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Attorney Docket No. 15966-534C CIP1 (CURA-534C CIP1)



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FIRST-NAMED INVENTOR:

Shimkets

FOR:

NUCLEIC ACIDS CONTAINING SINGLE NUCLEOTIDE POLYMORPHISMS AND METHODS OF USE THEREOF

December 27, 1999 Boston, Massachusetts

Box PATENT APPLICATION Assistant Commissioner for Patents Washington, D.C. 20231

REQUEST FOR FILING A CONTINUING UTILITY APPLICATION UNDER 37 C.F.R. §1.53(b)

1.	This is a request for filing a continuing application under 37 C.F.R. §1.53(b). (Check the appropriate boxes and supply the requisite information) This application is a: Continuation; Divisional; Continuation-in-part of prior application U.S.S.N. 09/442,849.				
2.		y to the above application(s) is claimed under:			
4.		35 U.S.C. §120			
		Prior application information:			
		Examiner: Not Yet Assigned; Group Art Unit: Not Yet Assigned.			
		35 U.S.C. §119			
		Priority of application Serial No, filed on in is claimed under			
		35 U.S.C. §119.			
		The certified copy has been filed in prior application U.S.S.N/, on [Date]. The certified copy will follow.			
APPL	ICATI(ON ELEMENTS:			
3.	\boxtimes	Specification and Drawings (Total pages: 265):			
		Specification(251 pages); Claims (12 pages); Abstract (1 page); and Drawings: 1 sheets; FIGS. 1.			
		Formal			
		Informal			
4.	\boxtimes	Nucleotide and/or Amino Acid Sequence Submission:			
		Computer-readable copy			
		Paper copy (identical to computer-readable copy)			
		Statement verifying paper copy identical to computer-readable copy			
5.		Microfiche Computer Program (Appendix)			
6.	\boxtimes	Oath or Declaration (Total pages: 3):			
	(a	Unsigned (original)			

FIRST-NAMED INVENTOR:

Shimkets Request for Continuing Nonprovisional Application (37 C.F.R. §1.53(b))

Claims		Number Basic Fee Number Rate Filed Allowance Extra	Basic Fee 37 C.F.R. 1.16(a) \$760.00		
		CLAIMS AS FILED			
		calculating the filing fee.	icitations prior to		
		A Preliminary Amendment is enclosed herewith. Please enter the claim amendments prior to			
11.	Fee Ca	Fee Calculation:			
	احسا	Copy of Statement filed in prior application (Status still proper an	d desired)		
10.		Statement Claiming Small Entity Status			
		Copy of IDS and PTO-1449 (pages) Copies of references cited			
9.		Information Disclosure Statement (IDS)			
8.		English Translation Document (if applicable)			
ACCC	OMPAN	YING APPLICATION PARTS:			
		The entire Disclosure of the prior application, from which a copy of the oar supplied under Box 6(b), is considered as being part of the disclosure of the application and is hereby incorporated by reference therein.			
7.		Incorporation by Reference (can use if Box 6(b) is checked)			
	(b	Copy from a prior application (37 C.F.R. §1.63(d))			

Claims	Number Filed	Basic Fee Allowance	Number Extra	Rate	Basic Fee 37 C.F.R. 1.16(a) \$760.00
Total Claims (37 C.F.R. 1.16(c))	44	- 20 =	24	\$ 18.00	\$432.00
Independent Claims (37 C.F.R. 1.16(b))	13	- 3 =	10	\$78.00	\$780.00
Multiple Dependent Claim(s), if any (37 C.F.R. 1.16(d))				\$260.00	0
			SUBTO	TAL:	\$1972.00
	Reduction	n by 50% for fil	ing by small e	entity:	- \$986.00
			TOTAL	FEE:	\$986.00

12.	\boxtimes	A check in the amount of \$986.00 is enclosed.
13.		Deletion of Inventor(s)
		This application is filed by fewer than all the inventors named in the prior application, 37 C.F.R. §1.53(d)(4).
		DELETE the following inventor(s) named in the prior nonprovisional application
		The inventor(s) to be deleted are set forth on a separate sheet attached hereto.

FIRST-NAMED INVENTOR: Shimkets				
Request for Continuing Nonprovisional Application (37 C.F.R. §1.53(b))				
			ommissioner is hereby authorized to credit overpayments or charge the ing fees to Deposit Account No. 50-0311, Ref. No. 15966-534C CIP1:	
			Fees required under 37 C.F.R. §1.16; Fees required under 37 C.F.R. §1.17; Fees required under 37 C.F.R. §1.18.	
15.	\boxtimes	Return Receipt Postcard Enclosed.		
16.	\boxtimes	Other 1	Documents Enclosed:	
			Change of Attorney Address In Application. Limited Recognition under 37 C.F.R. § 10.9(b) for Michel Morency.	
			Respectfully submitted,	
			Shelker & Walker	
Dated:	Decem	ber 27, 1	Ivor R. Elrifi, Reg. No. 39,529 Shelby J. Walker, Reg. No. 45,192 Attorney(s) for Applicants MINTZ, LEVIN, COHN, FERRIS, GLOVSKY and POPEO, P.C. One Financial Center Boston, Massachusetts 02111 Tel: (617) 542-6000 Fax: (617) 542-2241	
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PATENT APPLICATION ATTORNEY DOCKET NO. 15966-534C CIP1 (CURA-34 C CIP1)

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NUCLEIC ACIDS CONTAINING SINGLE NUCLEOTIDE POLYMORPHISMS AND METHODS OF USE THEREOF

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RELATED APPLICATIONS

This application is a continuation-in-part of U.S.S.N. 09/442,849, filed November 17, 1999, which claims priority to USSN 09/442,129 and USSN _____, both filed November 16, 1999, all of which are entitled "Nucleic Acids Containing Single Nucleotide Polymorphisms and Methods of Use Thereof" and naming Richard Shimkets and Martin Leach as inventors, and to USSN 60/109,024, filed November 17, 1998. The contents of these applications are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

The invention relates generally to nucleic acids and polypeptides and in particular to the identification of human single nucleotide polymorphisms based on at least one gene product that was not previously described.

BACKGROUND OF THE INVENTION

Sequence polymorphism-based analysis of nucleic acid is generally based on alterations in nucleic acid sequences between related individuals. This analysis has been widely used in a variety of genetic, diagnostic, and forensic applications. For example, polymorphism analyses are used in identity and paternity analysis, and in genetic mapping studies.

Several different types of polymorphisms in nucleic acid have been described.

One such type of variation is a restriction fragment length polymorphism (RFLP). RFLPS can create or delete a recognition sequence for a restriction endonuclease in one nucleic

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acid relative to a second nucleic acid. The result of the variation is in an alteration the relative length of restriction enzyme generated DNA fragments in the two nucleic acids.

Other polymorphisms take the form of short tandem repeats (STR) sequences, which are also referred to as variable numbers of tandem repeat (VNTR) sequences. STR sequences typically that include tandem repeats of 2, 3, or 4 nucleotide sequences that are present in a nucleic acid from one individual but absent from a second, related individual at the corresponding genomic location.

Other polymorphisms take the form of single nucleotide variations, termed single nucleotide polymorphisms (SNPs), between individuals. A SNP can, in some instances, be referred to as a "cSNP" to denote that the nucleotide sequence containing the SNP originates as a cDNA.

SNPs can arise in several ways. A single nucleotide polymorphism may arise due to a substitution of one nucleotide for another at the polymorphic site. Substitutions can be transitions or transversions. A transition is the replacement of one purine nucleotide by another purine nucleotide, or one pyrimidine by another pyrimidine. A transversion is the replacement of a purine by a pyrimidine, or the converse.

Single nucleotide polymorphisms can also arise from a deletion of a nucleotide or an insertion of a nucleotide relative to a reference allele. Thus, the polymorphic site is a site at which one allele bears a gap with respect to a single nucleotide in another allele. Some SNPs occur within, or near genes. One such class includes SNPs falling within regions of genes encoding for a polypeptide product. These SNPs may result in an alteration of the amino acid sequence of the polypeptide product and give rise to the expression of a defective or other variant protein. Such variant products can, in some cases result in a pathological condition, *e.g.*, genetic disease. Examples of genes in which a polymorphism within a coding sequence gives rise to genetic disease include sickle cell anemia and cystic fibrosis. Other SNPs do not result in alteration of the polypeptide product. Of course, SNPs can also occur in noncoding regions of genes.

SNPs tend to occur with great frequency and are spaced uniformly throughout the

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genome. The frequency and uniformity of SNPs means that there is a greater probability that such a polymorphism will be found in close proximity to a genetic locus of interest.

SUMMARY OF THE INVENTION

The invention is based in part on the discovery of single nucleotide polymorphisms (SNPs) in regions of human DNA.

Accordingly, in one aspect, the invention provides nucleic acid sequences comprising nucleic acid segments of both publicly known and novel genes, including the polymorphic site. The segments can be DNA or RNA, and can be single- or double-stranded. Preferred segments include a biallelic polymorphic site.

The invention further provides allele-specific oligonucleotides that hybridize to a segment of a fragment shown in Table 1, column 4, or its complement. These oligonucleotides can be probes or primers. Also provided are isolated nucleic acids comprising a sequence shown in Table 1, column 4, in which the polymorphic site within the sequence is occupied by a base other than the reference bases shown in Table 1, columns 5 and 6.

The invention further provides a method of analyzing a nucleic acid from an individual. The method determines which base is present at any one of the polymorphic sites shown in Table 1. Optionally, a set of bases occupying a set of polymorphic sites shown in Table 1 is determined. This type of analysis can be performed on a number of individuals, who are tested for the presence of a disease phenotype.

In another aspect, the invention provides an isolated polynucleotide which includes one or more of the SNPs described herein. The polynucleotide can be, e.g., a nucleotide sequence which includes one or more of the polymorphic sequences shown in Table 1 and which includes a polymorphic sequence, or a fragment of the polymorphic sequence, as long as it includes the polymorphic site. The polynucleotide may alternatively contain a nucleotide sequence which includes a sequence complementary to one or more of these sequences, or a fragment of the complementary nucleotide

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sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence.

The polynucleotide can be, *e.g.*, DNA or RNA, and can be between about 10 and about 100 nucleotides, *e.g.*, 10-90, 10-75, 10-51, 10-40, or 10-30, nucleotides in length.

In preferred embodiments, the polymorphic site in the polymorphic sequence includes a nucleotide other than the nucleotide listed in Table 1, column 5 for the polymorphic sequence, *e.g.*, the polymorphic site includes the nucleotide listed in Table 1, column 6 for the polymorphic sequence.

In other embodiments, the complement of the polymorphic site includes a nucleotide other than the complement of the nucleotide listed in Table 1, column 5 for the complement of the polymorphic sequence, *e.g.*, the complement of the nucleotide listed in Table 1, column 6 for the polymorphic sequence.

In some embodiments, the polymorphic sequence is associated with a polypeptide related to one of the protein families disclosed herein. For example, the nucleic acid may be associated with a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, or any of the other proteins identified in Table 1, column 10.

In another aspect, the invention provides an isolated allele-specific oligonucleotide that hybridizes to a first polynucleotide containing a polymorphic site. The first polynucleotide can be, *e.g.*, a nucleotide sequence comprising one or more polymorphic sequences recited in Table 1, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence. Alternatively, the first polynucleotide can be a nucleotide sequence that is a fragment of the polymorphic sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence, or a complementary nucleotide sequence which includes a sequence complementary to one or more polymorphic sequences in Table 1, provided that the complementary nucleotide sequence includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5. The first polynucleotide may in addition include a nucleotide sequence that is a fragment of

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the complementary sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence.

In some embodiments, the oligonucleotide does not hybridize under stringent conditions to a second polynucleotide. The second polynucleotide can be, e.g., (a) a nucleotide sequence comprising one or more polymorphic sequences in Table 1, wherein the polymorphic sequence includes the nucleotide listed in Table 1, column 5 for the polymorphic sequence; (b) a nucleotide sequence that is a fragment of any of the polymorphic sequences; (c) a complementary nucleotide sequence including a sequence complementary to one or more polymorphic sequences disclosed herein in Table 1; and (d) a nucleotide sequence that is a fragment of the complementary sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence.

The oligonucleotide can be, *e.g.*, between about 10 and about 100 bases in length. In some embodiments, the oligonucleotide is between about 10 and 75 bases, 10 and 51 bases, 10 and about 40 bases, or about 15 and 30 bases in length.

The invention also provides a method of detecting a polymorphic site in a nucleic acid. The method includes contacting the nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected shown in Table 1, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5. The method also includes determining whether the nucleic acid and the oligonucleotide hybridize. Hybridization of the oligonucleotide to the nucleic acid sequence indicates the presence of the polymorphic site in the nucleic acid.

In preferred embodiments, the oligonucleotide does not hybridize to the polymorphic sequence when the polymorphic sequence includes the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or when the complement of the polymorphic sequence includes the complement of the nucleotide recited in Table 1, column 5 for the polymorphic sequence.

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The oligonucleotide can be, *e.g.*, between about 10 and about 100 bases in length. In some embodiments, the oligonucleotide is between about 10 and 75 bases, 10 and 51 bases, 10 and about 40 bases, or about 15 and 30 bases in length.

In some embodiments, the polymorphic sequence identified by the oligonucleotide is associated with a nucleic acid encoding polypeptide related to one of the protein families disclosed herein. the polymorphic sequence is associated with a polypeptide related to one of the protein families disclosed herein. For example, the nucleic acid may be associated with a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, or any of the other proteins identified in Table 1, column 10.

In a further aspect, the invention provides a method of determining the relatedness of a first and second nucleic acid. The method includes providing a first nucleic acid and a second nucleic acid and contacting the first nucleic acid and the second nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected disclosed in Table 1, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5. The method also includes determining whether the first nucleic acid and the second nucleic acid hybridize to the oligonucleotide, and comparing hybridization of the first and second nucleic acids to the oligonucleotide. Hybridization of first and second nucleic acids to the nucleic acid indicates the first and second subjects are related.

In preferred embodiments, the oligonucleotide does not hybridize to the polymorphic sequence when the polymorphic sequence includes the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or when the complement of the polymorphic sequence includes the complement of the nucleotide recited in Table 1, column 5 column for the polymorphic sequence.

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The oligonucleotide can be, *e.g.*, between about 10 and about 100 bases in length. In some embodiments, the oligonucleotide is between about 10 and 75 bases, 10 and 51 bases, 10 and about 40 bases, or about 15 and 30 bases in length.

The method can be used in a variety of applications. For example, the first nucleic acid may be isolated from physical evidence gathered at a crime scene, and the second nucleic acid may be obtained is a person suspected of having committed the crime. Matching the two nucleic acids using the method can establishing whether the physical evidence originated from the person.

In another example, the first sample may be from a human male suspected of being the father of a child and the second sample may be from a child. Establishing a match using the described method can establishing whether the male is the father of the child.

In another aspect, the method includes determining if a sequence polymorphism is the present in a subject, such as a human. The method includes providing a nucleic acid from the subject and contacting the nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence disclosed in Table 1, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5. Hybridization between the nucleic acid and the oligonucleotide is then determined. Hybridization of the oligonucleotide to the nucleic acid sequence indicates the presence of the polymorphism in said subject.

In another aspect, the invention provides an isolated polypeptide comprising a polymorphic site at one or more amino acid residues, and wherein the protein is encoded by a polynucleotide including one of the polymorphic sequences in Table 1, or their complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5.

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The polypeptide can be, *e.g.*, related to one of the protein families disclosed herein. For example, polypeptide can be related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

In some embodiments, the polypeptide is translated in the same open reading frame as is a wild type protein whose amino acid sequence is identical to the amino acid sequence of the polymorphic protein except at the site of the polymorphism.

In some embodiments, the polypeptide encoded by the polymorphic sequence, or its complement, includes the nucleotide listed in Table 1, column 6 for the polymorphic sequence, or the complement includes the complement of the nucleotide listed in Table 1, column 6.

The invention also provides an antibody that binds specifically to a polypeptide encoded by a polynucleotide comprising a nucleotide sequence encoded by a polynucleotide including one or more of the polymorphic sequences in Table 1, or its complement. The polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5.

In some embodiments, the antibody binds specifically to a polypeptide encoded by a polymorphic sequence which includes the nucleotide listed in Table 1, column 6 for the polymorphic sequence.

Preferably, the antibody does not bind specifically to a polypeptide encoded by a polymorphic sequence which includes the nucleotide listed in Table 1, column 5 for the polymorphic sequence.

The invention further provides a method of detecting the presence of a polypeptide having one or more amino acid residue polymorphisms in a subject. The method includes providing a protein sample from the subject and contacting the sample with the above-described antibody under conditions that allow for the formation of

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antibody-antigen complexes. The antibody-antigen complexes are then detected. The presence of the complexes indicates the presence of the polypeptide.

The invention also provides a method of treating a subject suffering from, at risk for, or suspected of, suffering from a pathology ascribed to the presence of a sequence polymorphism in a subject, e.g., a human, non-human primate, cat, dog, rat, mouse, cow, pig, goat, or rabbit. The method includes providing a subject suffering from a pathology associated with aberrant expression of a first nucleic acid comprising a polymorphic sequence shown in Table 1, or its complement, and treating the subject by administering to the subject an effective dose of a therapeutic agent. Aberrant expression can include qualitative alterations in expression of a gene, e.g., expression of a gene encoding a polypeptide having an altered amino acid sequence with respect to its wild-type counterpart. Qualitatively different polypeptides can include, shorter, longer, or altered polypeptides relative to the amino acid sequence of the wild-type polypeptide. Aberrant expression can also include quantitative alterations in expression of a gene. Examples of quantitative alterations in gene expression include lower or higher levels of expression of the gene relative to its wild-type counterpart, or alterations in the temporal or tissuespecific expression pattern of a gene. Finally, aberrant expression may also include a combination of qualitative and quantitative alterations in gene expression.

The therapeutic agent can include, *e.g.*, second nucleic acid comprising the polymorphic sequence, provided that the second nucleic acid comprises the nucleotide present in the wild type allele. In some embodiments, the second nucleic acid sequence comprises a polymorphic sequence which includes nucleotide listed in Table 1, column 5 for the polymorphic sequence.

Alternatively, the therapeutic agent can be a polypeptide encoded by a polynucleotide comprising polymorphic sequence shown in Table 1, or by a polynucleotide comprising a nucleotide sequence that is complementary to any one of the polymorphic sequences, provided that the polymorphic sequence includes the nucleotide listed in Table 1, column 6 for the polymorphic sequence.

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The therapeutic agent may further include an antibody as herein described, or an oligonucleotide comprising a polymorphic sequence shown in Table 1, or by a polynucleotide comprising a nucleotide sequence that is complementary to any one the polymorphic sequences, provided that the polymorphic sequence includes the nucleotide listed in Table 1, column 6 for the polymorphic sequence,

In another aspect, the invention provides an oligonucleotide array comprising one or more oligonucleotides hybridizing to a first polynucleotide at a polymorphic site encompassed therein. The first polynucleotide can be, *e.g.*, a nucleotide sequence comprising one or more polymorphic sequences shown in Table 1; a nucleotide sequence that is a fragment of any of the nucleotide sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence; a complementary nucleotide sequence comprising a sequence complementary to one or more of the polymorphic sequences; or a nucleotide sequence that is a fragment of the complementary sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence.

In preferred embodiments, the array comprises 10; 100; 1,000; 10,000; 100,000 or more oligonucleotides.

The invention also provides a kit comprising one or more of the herein-described nucleic acids. The kit can include, *e.g.*, polynucleotide which includes one or more of the SNPs described herein. The polynucleotide can be, *e.g.*, a nucleotide sequence which includes one or more of the polymorphic sequences shown in Table 1, and which includes a polymorphic sequence, or a fragment of the polymorphic sequence, as long as it includes the polymorphic site. The polynucleotide may alternatively contain a nucleotide sequence which includes a sequence complementary to one or more of the sequences, or a fragment of the complementary nucleotide sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence.

Alternatively, or in addition, the kit can include the invention provides an isolated allele-specific oligonucleotide that hybridizes to a first polynucleotide containing a polymorphic site. The first polynucleotide can be, *e.g.*, a nucleotide sequence comprising one or more polymorphic sequences shown in Table 1, provided that the polymorphic

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sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for the polymorphic sequence. Alternatively, the first polynucleotide can be a nucleotide sequence that is a fragment of the polymorphic sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence, or a complementary nucleotide sequence which includes a sequence complementary to one or more polymorphic sequences shown in Table 1, provided that the complementary nucleotide sequence includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 6. The first polynucleotide may in addition include a nucleotide sequence that is a fragment of the complementary sequence, provided that the fragment includes a polymorphic site in the polymorphic sequence.

BRIEF DESCRIPTION OF THE DRAWING

FIG. 1 illustrates an example of the way in which SNP sites were identified in the present invention.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

DETAILED DESCRIPTION OF THE INVENTION

The invention provides human SNPs in sequences which are transcribed, *i.e.*, are cSNPs. Many SNPs have been identified in genes related to polypeptides of known

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function. If desired, SNPs associated with various polypeptides can be used together. For example, SNPs can be grouped according to whether they are derived from a nucleic acid encoding a polypeptide related to particular protein family or involved in a particular function. Similarly, SNPs can be grouped according to the functions played by their gene products. Such functions include, structural proteins, proteins from which associated with metabolic pathways fatty acid metabolism, glycolysis, intermediary metabolism, calcium metabolism, proteases, and amino acid metabolism, etc. Specifically, the present invention provides a large number of human cSNP's based on at least one gene product that has not been previously identified. In contrast, and as defined specifically in the following paragraph, the cSNP's involve nucleic acid sequences that are assembled from at least one known sequence.

The present invention describes 651 distinct polymorphic sites, which are summarized in Table 1. Raw traces underlying sequence data were drawn from public databases and from the proprietary database of the Assignee of the present invention. The sequences were obtained by calling the bases from these traces, and included assigning "Phred" quality scores for each called base. For each allelic set, at the polynucleotide level, four or more nucleotide sequences were identified having at least partial overlap with one another.

As illustrated in FIG. 1, these four or more sequences could be clustered and assembled to make a consensus contig that included an ORF. In this way, the inventors found that the assembled contigs defined associated sets of two, or possibly more than two, alleles defined by a SNP at a particular polymorphic site. In order to be confirmed as a SNP site, the nucleotide change from the consensus sequence had to occur in at least two individual sequences, and had to have a "Phred" score of 23 or higher at the site of the presumed SNP. Furthermore, in a window of 5 bases on either side of the SNP, no more than 50% mismatching with the consensus sequence was allowed. In the assembly leading to each of the contigs defining the allelic set, the SNP alleles occur in polynucleotides found in public databases.

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It was found that the assembled contigs defined associated sets of two, or possibly more than two, alleles defined by an SNP at a particular polymorphic site. These associations were not previously known.

At the level of translation of an ORF contained in the contigs, allelic sets were identified in which one allele defines a known polypeptide sequence that includes the polymorphic site and another polypeptide allele is not previously known. Then, various associations of alleles are possible. For example, it is possible that an allelic pair is defined in a noncoding region of the contig containing an ORF. In such cases the inventors believe that the invention resides in the recognition of the allelic pair; this association has not heretofore been made.

Alternatively, sets of allelic contigs may exist in which the polymorphic site is within an ORF, but does not result in an amino acid change among the allelic polypeptides. Thus, in another embodiment, the polymorphic site resides within an ORF and results in an amino acid change, or a frameshift, among the alleles of the allelic set. In the sets of gene products that fall within this group, at least one of the alleles at the polypeptide level is a known protein. At least one of the remaining allele or alleles in the set, carrying a variant amino acid at the polymorphic site, is a novel polypeptide not heretofore known. The invention resides at least in the recognition of the polymorphic allele as being a variant of the known reference polypeptide.

Table 1 provides information concerning the allelic sequences. One of the sequences may be termed a reference polymorphic sequence, and the corresponding second sequence includes the variant SNP at the polymorphic site. Since the reference polypeptide sequence is already known, the Sequence Listing accompanying this application provides only the sequence of the polymorphic allele, while its SEQ ID NO is provided in the Table. A reference to the SEQ ID NO that corresponds to the translated amino acid sequence is also given. The Table includes thirteen columns that provide descriptive information for each cSNP, each of which occupies one row in the Table. The column headings, and a description of each, are given below.

SNPs disclosed in Table 1 were detected by aligning large numbers of sequences from genetically diverse sources of publicly available mRNA libraries (Clontech). Software designed specifically to look for multiple examples of variant bases differing from a consensus sequence was created and deployed. A criteria of a minimum of 2 occurrences of a sequence differing from the consensus in high quality sequence reads was used to identify an SNP.

The SNPs described herein may be useful in diagnostic kits, for DNA arrays on chips and for other uses that involve hybridization of the SNP.

Specific SNPs may have utility where a disease has already been associated with that gene. Examples of possible disease correlations between the claimed SNPs with members of the genes of each classification are listed below:

Amylases

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Amylase is responsible for endohydrolysis of 1,4-alpha-glucosidic linkages in oligosaccharides and polysaccharides. Variations in amylase gene may be indicative of delayed maturation and of various amylase producing neoplasms and carcinomas.

Amyloid

The serum amyloid A (SAA) proteins comprise a family of vertebrate proteins that associate predominantly with high density lipoproteins (HDL). The synthesis of certain members of the family is greatly increased in inflammation. Prolonged elevation of plasma SAA levels, as in chronic inflammation, 15 results in a pathological condition, called amyloidosis, which affects the liver, kidney and spleen and which is characterized by the highly insoluble accumulation of SAA in these tissues. Amyloid selectively inhibits insulin-stimulated glucose utilization and glycogen deposition in muscle, while not affecting adipocyte glucose metabolism. Deposition of fibrillar amyloid proteins intraneuronally, as neurofibrillary tangles, extracellularly, as plaques and in blood vessels, is characteristic of both Alzheimer's disease and aged Down's syndrome. Amyloid deposition is also associated with type II diabetes mellitus.

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Members of the angiopoeitin/fibrinogen family have been shown to stimulate the generation of new blood vessels, inhibit the generation of new blood vessels, and perform several roles in blood clotting. This generation of new blood vessels, called angiogenesis, is also an essential step in tumor growth in order for the tumor to get the blood supply it needs to expand. Variation in these genes may be predictive of any form of heart disease, numerous blood clotting disorders, stroke, hypertension and predisposition to tumor formation and metastasis. In particular, these variants may be predictive of the response to various antihypertensive drugs and chemotherapeutic and anti-tumor agents.

Apoptosis-related proteins

Active cell suicide (apoptosis) is induced by events such as growth factor withdrawal and toxins. It is controlled by regulators, which have either an inhibitory effect on programmed cell death (anti-apoptotic) or block the protective effect of inhibitors (pro-apoptotic). Many viruses have found a way of countering defensive apoptosis by encoding their own anti-apoptosis genes preventing their target-cells from dying too soon. Variants of apoptosis related genes may be useful in formulation of anti-aging drugs.

Cadherin, Cyclin, Polymerase, Oncogenes, Histones, Kinases

Members of the cell division/cell cycle pathways such as cyclins, many transcription factors and kinases, DNA polymerases, histones, helicases and other oncogenes play a critical role in carcinogenesis where the uncontrolled proliferation of cells leads to tumor formation and eventually metastasis. Variation in these genes may be predictive of predisposition to any form of cancer, from increased risk of tumor formation to increased rate of metastasis. In particular, these variants may be predictive of the response to various chemotherapeutic and anti-tumor agents.

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Colony-stimulating factor-related proteins

Granulocyte/macrophage colony-stimulating factors are cytokines that act in hematopoiesis by controlling the production, differentiation, and function of 2 related white cell populations of the blood, the granulocytes and the monocytes-macrophages.

Complement-related proteins

Complement proteins are immune associated cytotoxic agents, acting in a chain reaction to exterminate target cells to that were opsonized (primed) with antibodies, by forming a membrane attack complex (MAC). The mechanism of killing is by opening pores in the target cell membrane. Variations in 20 complement genes or their inhibitors are associated with many autoimmune disorders. Modified serum levels of complement products cause edemas of various tissues, lupus (SLE), vasculitis, glomerulonephritis, renal failure, hemolytic anemia, thrombocytopenia, and arthritis. They interfere with mechanisms of ADCC (antibody dependent cell cytotoxicity), severely impair immune competence and reduce phagocytic ability. Variants of complement genes may also be indicative of type I diabetes mellitus, meningitis neurological disorders such as Nemaline myopathy, Neonatal hypotonia, muscular disorders such as congenital myopathy and other diseases.

Cytochrome

The respiratory chain is a key biochemical pathway which is essential to all aerobic cells. There are five different cytochromes involved in the chain. These are heme bound proteins which serve as electron carriers. Modifications in these genes may be predictive of ataxia areflexia, dementia and myopathic and neuropathic changes in muscles. Also, association with various types of solid tumors.

Kinesins

Kinesins are tubulin molecular motors that function to transport organelles within cells and to move chromosomes along microtubules during cell division. Modifications of

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these genes may be indicative of neurological disorders such as Pick disease of the brain, tuberous sclerosis.

Cytokines, Interferon, Interleukin

Members of the cytokine families are known for their potent ability to stimulate cell growth and division even at low concentrations. Cytokines such as erythropoietin are cell-specific in their growth stimulation; erythropoietin is useful for the stimulation of the proliferation of erythroblasts. Variants in cytokines may be predictive for a wide variety of diseases, including cancer predisposition.

G-protein coupled receptors

G-protein coupled receptors (also called R7G) are an extensive group of hormones, neurotransmitters, odorants and light receptors which transduce extracellular signals by interaction with guanine nucleotide-binding (G) proteins. Alterations in genes coding for G-coupled proteins may be involved in and indicative of a vast number of physiological conditions. These include blood pressure regulation, renal dysfunctions, male infertility, dopamine associated cognitive, emotional, and endocrine functions, hypercalcemia, chondrodysplasia and osteoporosis, pseudohypoparathyroidism, growth retardation and dwarfism.

Thioesterases

Eukaryotic thiol proteases are a family of proteolytic enzymes which contain an active site cysteine. Catalysis proceeds through a thioester intermediate and is facilitated by a nearby histidine side chain; an asparagine completes the essential catalytic triad. Variants of thioester associated genes may be predictive of neuronal disorders and mental illnesses such as Ceroid Lipoffiscinosis, Neuronal 1, Infantile, Santavuori disease and more.

Breakdown Classifications of SNPS

The following list describes the numerical breakdown by molecule type of the SNPs described in Table 1. The key to these molecule types is as follows.

5		
	TPase associated:	864
	Guanylyl:	3
	MHC:	1077
	amylase:	44
10	amylaseinhib:	1
	amyloid:	96
	apoptosis:	91
	apoptosisinhib:	29
	apoptosisrecep:	14
15	biotindep:	29
	cadhenn:	415
	calcium_channel:	85
	carboxylase:	4
	cathepsin:	336
20	cathepsininhib:	41
	chloride_channel:	90
	collagen:	1542
	complement:	222
	complementinhib:	21
25	complementrecept:	10
	csf:	31
	csf recept:	37
	cyclin:	65
	cyto45O:	136
30	cytochrome:	659
	deaminase:	44
•	dehydrogenase:	1235
	desaturase:	9
	dna_rna_bind:	1309
35	dna_rna_bind_inhib:	16
	dynein:	108
	elastase:	134
	elastaseinhib:	6
	eph:	487
40	esterase:	258
	esteraseinhib:	3
	fgf:	34
	fgf receptor:	12
	gaba:	45
45	glucoamylase:	106
	glucuronidase:	14
	glycoprotein:	3176
	helicase:	333
	histone:	272
50	homeobox:	431
	hydrolase:	187

5	hydroxysteroid:	84
•	hypoxanthine:	4
	immunoglob:	1106
	immunoglob_recept:	19
	interferon:	322
10	interleukin:	88
10	interleukinrecept:	126
	isomerase:	404
	isomeraseinhibitor:	45
	isomerasereceptor:	4
15	kinase:	1684
15	kinase inhibitor:	187
		233
	kinase receptor: kinesin:	86
	laminin:	196
20		63
20	lipase: metallothionein:	62
		215
	misc_channel:	30
	ngf:	339
25	nucl_recpt: nuclease:	298
25		783
	oncogene: oxidase:	128
		14
	oxygenase: peptidase:	150
20	peroxidase:	115
30	phosphatase:	668
	phosphataseinhib:	71
		84
	phosphorylase: polymerase:	489
25	potassium channel:	43
35	prostaglandin:	55
	prostagramm. protease:	954
	protease. proteaseinhib:	271
	reductase:	243
40	ribosomal prot:	1040
40	struct:	3128
	sulfotransferase:	42
	synthase:	893
	•	117
	tgf:	41
45	tgfreceptor: thioesterase:	3
		38
	thiolase:	453
	tm7: tnf:	151
50		36
50	tnfreceptor:	30

5	traffic:	22
	transcriptfactor:	1139
	transferase:	291
	transport:	900
	tubulin:	334
10	ubiquitin:	229
	water channel:	18
	unclassified:	10567

The key to the molecule type is as follows:

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	Abbrev:	Title:
	amylase	amylase protein
	amylaseinhib	amylase inhibitor
20	amyloid	amyloid protein
	apoptosis	apoptosis associated protein
	apoptosisinhib	apoptosis inhibitors
	apoptosisrecep	apoptosis receptors
	ATPase_associated	ATPase associated protein
25	biotindep	biotin dependent enzyme/protein
	cadherin	cadherin protein
	calcium_channel	calcium channel protein
	carboxylase	carboxylase protein
	cathepsin	cathepsin/carboxypeptidases
30	cathepsininhib	cathepsin/carboxypeptidase inhibitor
	chloride_channel	chloride channel protein
	collagen	collagen
	complement	complement protein
	complementrecept	complement receptor protein
35	complementinhib	complement inhibitor
	csf	colony stimulating factor
	csfrecept	colony stimulating factor receptor
	cyclin	cyclin protein
	cyto450	cytochrome p450 protein
40	cytochrome	cytochrome related protein
	deaminase	deaminase
	dehydrogenase	dehydrogenase
	desaturase	desaturase
	dna_rna_bind	DNA/RNA binding protein/factor
45	dna_rna_inhib	DNA/RNA binding protein/factor
		inhibitor
	dynein	dynein
	elastase	elastase

5	elastaseinhib	elastase inhibitor
J	eph	EPH family of tyrosine kinases
	esterase	esterase
	esteraseinhib	esterase inhibitor
	fgf	fibroblast growth factor
10	fgfreceptor	fibroblast growth factor receptor
10		GABA receptor
	gaba	glucoamylase
	glucoamylase	glucoronidase
	glucoronidase	glycoprotein
	glycoprotein	guanylylate cyclase
15	Guanylyl	helicase
	helicase	histone
	histone	
	HOM	homologous
	homeobox	homeobox protein
20	hydrolase	hydrolase
	hydroxysteroid	hydroxysteroid associated protein
	hypoxanthine	hypoxanthine associated protein
	immunoglob	immunoglobulin
	immunoglobrecept	immunoglobulin receptor
25	interferon	interferon
	interleukin	interleukin
	interleukinrecept	interleukin receptor
	isomerase	isomerase
	isomeraseinhibitor	isomerase inhibitor
30	isomerasereceptor	isomerase receptor
	kinase	kinase
	kinaseinhibitor	kinase inhibitor
	kinasereceptor	kinase receptor
	kinesin	kinesin
35	laminin	laminin associated protein
	lipase	lipase
	metallothionein	metallothionein
	MHC	major histocompatability complex
	misc_channel	miscellaneous channel
40	ngf	nerve growth factor
	nuci_recpt	nuclear receptor
	nuclease	nuclease
	oncogene	oncogene associated protein
	oxidase	oxidase
45	oxygenase	oxygenase
	peptidase	peptidase
	peroxidase	peroxidase
	phosphatase	phosphatase
	phosphataseinhib	phosphatase inhibitor
50	phosphorylase	phosphorylase
2.3	L\	* * *

5	PIR	PIR DATABASE (release 56, 29-OCT-1998)
	polymerase	polymerase
	potassium channel	potassium channel protein
	prostaglandin	prostaglandin
10	protease	protease
10	proteaseinhib	protease inhibitor
	reductase	reductase
	ribosomalprot	ribosomal associated protein
	RTR	EMBLDATABASE translated
15		entries not to be incorporated into
10		SWISS-PROT (20-JUL-1998)
	SIM	similar
	SPTR	EMBL DATABASE translated
		entries to be incorporated into
20		SWISS-PROT (20-JUL-1998)
	struct	structural associated protein
	sulfotransferase	sulfotransferase
	SWP	SWISS-PROT DATABASE (release
		18-OCT-1998)
25	SWPN	SWISS-PROT Update (release 11-
	_	NOV-98)
	synthase	synthase
	tgf	transforming growth factor
	tgfreceptor	transforming growth factor receptor thioesterase
30	thioesterase	thiolase
	thiolase	seven transmembrane domain G-
	tm7	protein coupled receptor
	tnf	necrosis factor receptor
35	traffic	tumor necrosis factor
33	tnfreceptor	tumor trafficking associated protein
	TRN	EMBL DATABASE translated
		entries update (20-JUL-1998)
	transcriptfactor	transcription factor
40	transferase	transferase
. •	transport	transport protein
	tubulin	tubulin
	ubiquitin	ubiquitin
	unclassified	Protein not categorized into one of
45		the aforementioned protein families
	water channel	water channel protein

Table 1

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A compilation of polymorphisms is listed in Table 1. Table 1 includes thirteen columns that provide descriptive information for each cSNP, each of which occupies one row in the Table. The column headings, and an explanation for each, are given below.

The first column of the table lists the names assigned to the fragments in which the polymorphisms occur. The fragments are all human genomic fragments. The sequence of one allelic form of each of the fragments (arbitrarily referred to as the prototypical or reference form) has been previously published. These sequences are listed at http://www-genome.wi.mit.edu/ (all STS's sequence tag sites)); http://shgc.stanford.edu (Stanford STS's); and http://www.tigr.org/ (TIGR STS's). The web sites also list primers for amplification of the fragments, and the genomic location of the fragments. Some fragments are expressed sequence tags, and some are random genomic fragments. All information in the web sites concerning the fragments listed in the table is incorporated by reference in its entirety for all purposes.

The second column lists the position in the fragment in which a polymorphic site has been found. Positions are numbered consecutively with the first base of the fragment sequence listed as in one of the above databases being assigned the number one. The third column lists the base occupying the polymorphic site in the sequence in the data base. This base is arbitrarily designated the reference or prototypical form, but it is not necessarily the most frequently occurring form. The fourth column in the table lists the alternative base(s) at the polymorphic site. The fifth column of the table lists a 5' (upstream or forward) primer that hybridizes with the 5' end of the DNA sequence to be amplified. The sixth column of the table lists a 3' (downstream or reverse) primer that hybridizes with the complement of the 3' end of the sequence to be amplified. The seventh column of the table lists a number of bases of sequence on either side of the polymorphic site in each fragment. The indicated sequences can either be DNA or RNA. In the latter, the T's shown in the table are replaced by U's. The base occupying the polymorphic site is indicated in EUT'AC-IUB ambiguity code.

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"SEQ ID" provides the cross-references to the two nucleotide SEQ ID NOS: for the cognate pair, which are numbered consecutively, and, as explained below, amino acid SEQ ID NOS: as well, in the Sequence Listing of the application.

Each sequence entry in the Sequence Listing also includes a cross-reference to the CuraGen sequence ID, under the label "Accession number". The first pair of SEQ ID NOS: given in the first column of each row of the Table is the SEQ ID NO: identifying the nucleic acid sequence for the polymorphism. If a polymorphism carries an entry for the amino acid portion of the row, a third SEQ ID NO: appears in parentheses in the column "Amino acid before" (see below) for the reference amino acid sequence, and a fourth SEQ ID NO: appears in parentheses in the column "Amino acid after" (see below) for the polymorphic amino acid sequence. The latter SEQ ID NOS: refer to amino acid sequences giving the cognate reference and polymorphic amino acid sequences that are the translation of the nucleotide polymorphism. If a polymorphism carries no entry for the protein portion of the row, only one pair SEQ ID NOS: is provided, in the first column.

"CuraGen sequence ID" provides CuraGen Corporation's accession number.

"Base pos. of SNP" gives the numerical position of the nucleotide in the nucleic acid at which the cSNP is found, as identified in this invention.

"Polymorphic sequence" provides a 51-base sequence with the polymorphic site at the 26th base in the sequence, as well as 25 bases from the reference sequence on the 5' side and the 3' side of the polymorphic site. The designation at the polymorphic site is enclosed in square brackets, and provides first, the reference nucleotide; second, a "slash (/)"; and third, the polymorphic nucleotide. In certain cases the polymorphism is an insertion or a deletion. In that case, the position that is "unfilled" (i.e., the reference or the polymorphic position) is indicated by the word "gap".

"Base before" provides the nucleotide present in the reference sequence at the position at which the polymorphism is found.

"Base after" provides the altered nucleotide at the position of the polymorphism.

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"Amino acid before" provides the amino acid in the reference protein, if the polymorphism occurs in a coding region. This column also includes the SEQ ID NO: in parentheses for the translated reference amino acid sequence if the polymorphism occurs in a coding region.

"Amino acid after" provides the amino acid in the polymorphic protein, if the polymorphism occurs in a coding region. This column also includes the SEQ ID NO in parentheses for the translated polymorphic amino acid sequence if the polymorphism occurs in a coding region.

"Type of change" provides information on the nature of the polymorphism.

"SILENT-NONCODING" is used if the polymorphism occurs in a noncoding region of a nucleic acid. "SILENT-CODING" is used if the polymorphism occurs in a coding region of a nucleic acid of a nucleic acid and results in no change of amino acid in the translated polymorphic protein. "CONSERVATIVE" is used if the polymorphism occurs in a coding region of a nucleic acid and provides a change in which the altered amino acid falls in the same class as the reference amino acid. The classes are: 1) Aliphatic: Gly, Ala, Val, Leu, Ile; 2) Aromatic: Phe, Tyr, Trp; 3) Sulfur-containing: Cys, Met; 4) Aliphatic OH: Ser, Thr; 5) Basic: Lys, Arg, His; 6) Acidic: Asp, Glu, Asn, Gln; 7) Pro falls in none of the other classes; and 8) End defines a termination codon.

"NONCONSERVATIVE" is used if the polymorphism occurs in a coding region of a nucleic acid and provides a change in which the altered amino acid falls in a different class than the reference amino acid.

"FRAMESHIFT" relates to an insertion or a deletion. If the frameshift occurs in a coding region, the Table provides the translation of the frameshifted codons 3' to the polymorphic site.

"Protein classification of CuraGen gene" provides a generic class into which the protein is classified. Multiple classes of proteins were identified as listed above in the discussion of Table 1.

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"Name of protein identified following a BLASTX analysis of the CuraGen sequence" provides the database reference for the protein found to resemble the novel reference-polymorphism cognate pair most closely.

"Similarity (pvalue) following a BLASTX analysis" provides the pvalue, a statistical measure from the BLASTX analysis that the polymorphic sequence is similar to, and therefore an allele of, the reference, or wild-type, sequence. In the present application, a cutoff of pvalue $> 1 \times 10^{-50}$ (entered, for example, as 1.0E-50 in the Table) is used to establish that the reference-polymorphic cognate pairs are novel. A pvalue $< 1 \times 10^{-50}$ defines proteins considered to be already known.

"Map location" provides any information available at the time of filing related to localization of a gene on a chromosome.

The polymorphisms are arranged in Table 1 in the following order:

SEQ ID NOs: 1-422 are nucleotide sequences for SNPs that are silent.

SEQ ID NOs: 423-480 are nucleotide sequences for SNPs that lead to conservative amino acid changes.

SEQ ID NOs: 481-619 are nucleotide sequences for SNPs that lead to nonconservative amino acid changes.

SEQ ID NOs: 620-651 are nucleotide sequences for SNPs that involve a gap. With respect to the reference or wild-type sequence at the position of the polymorphism, the allelic cSNP introduces an additional nucleotide (an insertion) or deletes a nucleotide (a deletion). An SNP that involves a gap generates a frame shift.

Also presented in the sequence listing filed herewith are predicted amino acid sequences encoded by the polymorphic sequences shown in Table 1.

SEQ ID NOs: 652-709 are the amino acid sequences centered at the polymorphic amino acid residue for the protein products provided by SNPs that lead to conservative amino acid changes. 7 or 8 amino acids on either side of the polymorphic site are shown.

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The order in which these sequences appear mirrors the order of presentation of the cognate nucleotide sequences, and is set forth in the Table.

SEQ ID NOs: 710-848 are the amino acid sequences centered at the polymorphic amino acid residue for the protein products provided by SNPs that lead to nonconservative amino acid changes. 7 or 8 amino acids on either side of the polymorphic site are shown. The order in which these sequences appear mirrors the order of presentation of the cognate nucleotide sequences, and is set forth in the Table.

SEQ ID NOs: 849-880 are the amino acid sequences centered at the polymorphic amino acid residue for the protein products provided by SNPs that lead to frameshift-induced amino acid changes. 7 or 8 amino acids on either side of the polymorphic site are shown. The order in which these sequences appear mirrors the order of presentation of the cognate nucleotide sequences, and is set forth in the Table.

Provided herein are compositions which include, or are capable of detecting, nucleic acid sequences having these polymorphisms, as well as methods of using nucleic acids.

20 Identification of Individuals Carrying SNPs

Individuals carrying polymorphic alleles of the invention may be detected at either the DNA, the RNA, or the protein level using a variety of techniques that are well known in the art. Strategies for identification and detection are described in *e.g.*, EP 730,663, EP 717,113, and PCT US97/02102. The present methods usually employ precharacterized polymorphisms. That is, the genotyping location and nature of polymorphic forms present at a site have already been determined. The availability of this information allows sets of probes to be designed for specific identification of the known polymorphic forms.

Many of the methods described below require amplification of DNA from target samples. This can be accomplished by e.g., PCR. (1989), B. for detecting polymorphisms. See generally PCR Technology: Principles and Applications for DNA Amplification (ed. H.A. Erlich, Freeman Press, NY, NY, 1992); PCR Protocols: A

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Guide to Methods and Applications (eds. Innis, et al., Academic Press, San Diego, CA, 1990); Mattila et al., Nucleic Acids Res. 19, 4967 (1991); Eckert et al., PCR Methods and Applications 1, 17 (1991); PCR (eds. McPherson et al., IRL Press, Oxford); and U.S. Patent 4,683,202.

The phrase "recombinant protein" or "recombinantly produced protein" refers to a peptide or protein produced using non-native cells that do not have an endogenous copy of DNA able to express the protein. In particular, as used herein, a recombinantly produced protein relates to the gene product of a polymorphic allele, i.e., a "polymorphic protein" containing an altered amino acid at the site of translation of the nucleotide polymorphism. The cells produce the protein because they have been genetically altered by the introduction of the appropriate nucleic acid sequence. The recombinant protein will not be found in association with proteins and other subcellular components normally associated with the cells producing the protein. The terms "protein" and "polypeptide" are used interchangeably herein.

The phrase "substantially purified" or "isolated" when referring to a nucleic acid, peptide or protein, means that the chemical composition is in a milieu containing fewer, or preferably, essentially none, of other cellular components with which it is naturally associated. Thus, the phrase "isolated" or "substantially pure" refers to nucleic acid preparations that lack at least one protein or nucleic acid normally associated with the nucleic acid in a host cell. It is preferably in a homogeneous state although it can be in either a dry or aqueous solution. Purity and homogeneity are typically determined using analytical chemistry techniques such as gel electrophoresis or high performance liquid chromatography. Generally, a substantially purified or isolated nucleic acid or protein will comprise more than 80% of all macromolecular species present in the preparation. Preferably, the nucleic acid or protein is purified to represent greater than 90% of all macromolecular species present. More preferably the nucleic acid or protein is purified to greater than 95%, and most preferably the nucleic acid or protein is purified to essential homogeneity, wherein other macromolecular species are not detected by conventional analytical procedures.

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The genomic DNA used for the diagnosis may be obtained from any nucleated cells of the body, such as those present in peripheral blood, urine, saliva, buccal samples, surgical specimen, and autopsy specimens. The DNA may be used directly or may be amplified enzymatically in vitro through use of PCR (Saiki et al. Science 239:487-491 (1988)) or other in vitro amplification methods such as the ligase chain reaction (LCR) (Wu and Wallace Genomics 4:560-569 (1989)), strand displacement amplification (SDA) (Walker et al. Proc. Natl. Acad. Sci. U.S.A, 89:392-396 (1992)), self-sustained sequence replication (3SR) (Fahy et al. PCR Methods P&J& 1:25-33 (1992)), prior to mutation analysis.

The method for preparing nucleic acids in a form that is suitable for mutation detection is well known in the art. A "nucleic acid" is a deoxyribonucleotide or ribonucleotide polymer in either single-or double-stranded form, including known analogs of natural nucleotides unless otherwise indicated. The term "nucleic acids", as used herein, refers to either DNA or RNA. "Nucleic acid sequence" or "polynucleotide sequence" refers to a single-stranded sequence of deoxyribonucleotide or ribonucleotide bases read from the 5' end to the 3' end. The direction of 5' to 3' addition of nascent RNA transcripts is referred to as the transcription direction; sequence regions on the DNA strand having the same sequence as the RNA and which are beyond the 5' end of the RNA transcript in the 5' direction are referred to as "upstream sequences"; sequence regions on the DNA strand having the same sequence as the RNA and which are beyond the 3' end of the RNA transcript in the 3' direction are referred to as "downstream sequences". The term includes both self-replicating plasmids, infectious polymers of DNA or RNA and nonfunctional DNA or RNA. The complement of any nucleic acid sequence of the invention is understood to be included in the definition of that sequence. "Nucleic acid probes" may be DNA or RNA fragments.

The detection of polymorphisms in specific DNA sequences, can be accomplished by a variety of methods including, but not limited to, restriction-fragment-length-polymorphism detection based on allele-specific restriction-endonuclease cleavage (Kan and Dozy <u>Lancet</u> ii:910-912 (1978)), hybridization with allele-specific oligonucleotide probes (Wallace et al. Nucl. Acids Res. 6:3543-3557 (1978)), including immobilized

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oligonucleotides (Saiki et al. Proc. Natl. Acad. SCI. USA, 86:6230-6234 (1969)) or oligonucleotide arrays (Maskos and Southern Nucl. Acids Res 21:2269-2270 (1993)), allele-specific PCR (Newton et al. Nucl Acids Res 17:2503-2516 (1989)), mismatchrepair detection (MRD) (Faham and Cox Genome Res 5:474-482 (1995)), binding of MutS protein (Wagner et al. Nucl Acids Res 23:3944-3948 (1995), denaturing-gradient gel electrophoresis (DGGE) (Fisher and Lerman et al. Proc. Natl. Acad. Sci. U.S.A. 80:1579-1583 (1983)), single-strand-conformation-polymorphism detection (Orita et al. Genomics 5:874-879 (1983)), RNAase cleavage at mismatched base-pairs (Myers et al. Science 230:1242 (1985)), chemical (Cotton et al. Proc. Natl. w Sci. U.S.A, 8Z4397-4401 (1988)) or enzymatic (Youil et al. Proc. Natl. Acad. Sci. <u>U.S.A.</u> 92:87-91 (1995)) cleavage of heteroduplex DNA, methods based on allele specific primer extension (Syvanen et al. Genomics 8:684-692 (1990)), genetic bit analysis (GBA) (Nikiforov et al. &&I Acids 22:4167-4175 (1994)), the oligonucleotide-ligation assay (OLA) (Landegren et al. Science_241:1077 (1988)), the allele-specific ligation chain reaction (LCR) (Barrany Proc. Natl. Acad. Sci. U.S.A. 88:189-1 93 (1991)), gap-LCR (Abravaya et al. Nucl Acids Res 23:675-682 (1995)), radioactive and/or fluorescent DNA sequencing using standard procedures well known in the art, and peptide nucleic acid (PNA) assays (Orum et al., Nucl. Acids Res, 21:5332-5356 (1993); Thiede et al., Nucl. Acids Res. 24:983-984 (1996)).

"Specific hybridization" or "selective hybridization" refers to the binding, or duplexing, of a nucleic acid molecule only to a second particular nucleotide sequence to which the nucleic acid is complementary, under suitably stringent conditions when that sequence is present in a complex mixture (e.g., total cellular DNA or RNA). "Stringent conditions" are conditions under which a probe will hybridize to its target subsequence, but to no other sequences. Stringent conditions are sequence-dependent and are different in different circumstances. Longer sequences hybridize specifically at higher temperatures than shorter ones. Generally, stringent conditions are selected such that the temperature is about 5°C lower than the thermal melting point (Tm) for the specific sequence to which hybridization is intended to occur at a defined ionic strength and pH. The Tm is the temperature (under defined ionic strength, pH, and nucleic acid concentration) at which 50% of the target sequence hybridizes to the complementary

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probe at equilibrium. Typically, stringent conditions include a salt concentration of at least about 0.01 to about 1.0 M Na ion concentration (or other salts), at pH 7.0 to 8.3. The temperature is at least about 30°C for short probes (e.g., 10 to 50 nucleotides). Stringent conditions can also be achieved with the addition of destabilizing agents such as formamide. For example, conditions of 5X SSPE (750 mM NaCl, 50 mM NaPhosphate, 5 mM EDTA, pH 7.4) and a temperature of 25-30°C are suitable for allele-specific probe hybridizations.

"Complementary" or "target" nucleic acid sequences refer to those nucleic acid sequences which selectively hybridize to a nucleic acid probe. Proper annealing conditions depend, for example, upon a probe's length, base composition, and the number of mismatches and their position on the probe, and must often be determined empirically. For discussions of nucleic acid probe design and annealing conditions, see, for example, Sambrook et al., or <u>Current Protocols in Molecular Biology</u>, F. Ausubel *et* al., ed., Greene Publishing and Wiley-Interscience, New York (1987).

A perfectly matched probe has a sequence perfectly complementary to a particular target sequence. The test probe is typically perfectly complementary to a portion of the target sequence. A "polymorphic" marker or site is the locus at which a sequence difference occurs with respect to a reference sequence. Polymorphic markers include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The reference allelic form may be, for example, the most abundant form in a population, or the first allelic form to be identified, and other allelic forms are designated as alternative, variant or polymorphic alleles. The allelic form occurring most frequently in a selected population is sometimes referred to as the "wild type" form, and herein may also be referred to as the "reference" form. Diploid organisms may be homozygous or heterozygous for allelic forms. A diallelic polymorphism has two distinguishable forms (i.e., base sequences), and a triallelic polymorphism has three such forms.

As use herein an "oligonucleotide" is a single-stranded nucleic acid ranging in

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length from 2 to about 60 bases. Oligonucleotides are often synthetic but can also be produced from naturally occurring polynucleotides. A probe is an oligonucleotide capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing via hydrogen bond formation. Oligonucleotides probes are often between 5 and 60 bases, and, in specific embodiments, may be between 10-40, or 15-30 bases long. An oligonucleotide probe may include natural (i.e. A, G, C, or T) or modified bases (7-deazaguanosine, inosine, etc.). In addition, the bases in an oligonucleotide probe may be joined by a linkage other than a phosphodiester bond, such as a phosphoramidite linkage or a phosphorothioate linkage, or they may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than by phosphodiester bonds, so long as it does not interfere with hybridization. Examples of an oligonucleotide are shown in Table 1. Oligonucleotides can be all of a nucleic acid segment as represented in column 4 of Table 1; a nucleic acid sequence which comprises a nucleic acid segment represented in column 4 of Table 1 and additional nucleic acids (present at either or both ends of a nucleic acid segment of column 4); or a portion (fragment) of a nucleic acid segment represented in column 4 of the table which includes a polymorphic site. Preferred polymorphic sites of the invention include segments of DNA or their complements, which include any one of the polymorphic sites shown in the Table. The segments can be between 5 and 250 bases, and, in specific embodiments are between 5-10, 5-20, 10-20, 10-50, 20-50 or 10-100 bases. The polymorphic site can occur within any position of the segment. The segments can be from any of the allelic forms of the DNA shown in the Table.

As used herein, the term "primer" refers to a single-stranded oligonucleotide which acts as a point of initiation of template-directed DNA synthesis under appropriate conditions (e.g., in the presence of four different nucleoside triphosphates and a polymerization agent, such as DNA polymerase, RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30 nucleotides. Short primer molecules generally require cooler temperatures to form sufficiently stable hybrid complexes with the template. A primer need not be perfectly complementary to the exact sequence of the template, but should be sufficiently

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complementary to hybridize with it. The term "primer site" refers to the sequence of the target DNA to which a primer hybridizes. The term "primer pair" refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

DNA fragments can be prepared, for example, by digesting plasmid DNA, or by use of PCR. Oligonucleotides for use as primers or probes are chemically synthesized by methods known in the field of the chemical synthesis of polynucleotides, including by way of non-limiting example the phosphoramidite method described by Beaucage and Carruthers, Tetrahedron Lett 22:1859-1 862 (1981) and the triester method provided by Matteucci, et al., J. Am. Chem. Soc., 103:3185 (1981) both incorporated herein by reference. These syntheses may employ an automated synthesizer, as described in Needham-VanDevanter, D.R., et al., Nucleic Acids Res. 12:61596168 (1984). Purification of oligonucleotides may be carried out by either native acrylamide gel electrophoresis or by anion-exchange HPLC as described in Pearson, J.D. and Regnier, F.E., J. Chrom., 255:137-149 (1983). A double stranded fragment may then be obtained, if desired, by annealing appropriate complementary single strands together under suitable conditions or by synthesizing the complementary strand using a DNA polymerase with an appropriate primer sequence. Where a specific sequence for a nucleic acid probe is given, it is understood that the complementary strand is also identified and included. The complementary strand will work equally well in situations where the target is a double-stranded nucleic acid.

The sequence of the synthetic oligonucleotide or of any nucleic acid fragment can be can be obtained using either the dideoxy chain termination method or the Maxam-Gilbert method (see Sambrook et al. Molecular Cloning - a Laboratory Manual (2nd Ed.), Vols. 1-3, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, (1989), which is incorporated herein by reference. This manual is hereinafter referred to as "Sambrook et al."; Zyskind et al., (1988)). Recombinant DNA Laboratory Manual, (Acad. Press, New York). Oligonucleotides useful in diagnostic assays are typically at least 8 consecutive nucleotides in length, and may range upwards of 18 nucleotides in

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5 length to greater than 100 or more consecutive nucleotides.

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the SNP-containing nucleotide sequences of the invention, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, about 25, about 50, or about 60 nucleotides or an entire SNP coding strand, or to only a portion thereof.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a polymorphic nucleotide sequence of the invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences disclosed herein, antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. For example, the antisense nucleic acid molecule can generally be complementary to the entire coding region of an mRNA, but more preferably as embodied herein, it is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of the mRNA. An antisense oligonucleotide can range in length between about 5 and about 60 nucleotides, preferably between about 10 and about 45 nucleotides, more preferably between about 15 and 40 nucleotides, and still more preferably between about 15 and 30 in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using

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procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a polymorphic protein to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementary to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific

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interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual -u nits, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res* 15: 6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res* 15: 6131-6148) or a chimeric RNA -DNA analogue (Inoue *et al.* (1987) *FEBS Lett* 215: 327-330).

The following terms are used to describe the sequence relationships between two or more nucleic acids or polynucleotides: "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity", and "substantial identity". A "reference sequence" is a defined sequence used as a basis for a sequence comparison; a reference sequence may be a subset of a larger sequence, for example, as a segment of a full-length cDNA or gene sequence given in a sequence listing, or may comprise a complete cDNA or gene sequence. Optimal alignment of sequences for aligning a comparison window may, for example, be conducted by the local homology algorithm of Smith and Waterman Adv. Appl. Math., 2482 (1981), by the homology alignment algorithm of Needleman and Wunsch J. Mol. Biol. 48:443 (1970), by the search for similarity method of Pearson and Lipman Proc. Natl. Acad. Sci. U.S.A. 852444 (1988), or by computerized implementations of these algorithms (for example, GAP,

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5 BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Dr., Madison, WI).

Techniques for nucleic acid manipulation of the nucleic acid sequences harboring the cSNP's of the invention, such as subcloning nucleic acid sequences encoding polypeptides into expression vectors, labeling probes, DNA hybridization, and the like, are described generally in Sambrook et al., The phrase "nucleic acid sequence encoding" refers to a nucleic acid which directs the expression of a specific protein, peptide or amino acid sequence. The nucleic acid sequences include both the DNA strand sequence that is transcribed into RNA and the RNA sequence that is translated into protein, peptide or amino acid sequence. The nucleic acid sequences include both the full length nucleic acid sequences disclosed herein as well as non-full length sequences derived from the full length protein. It being further understood that the sequence includes the degenerate codons of the native sequence or sequences which may be introduced to provide codon preference in a specific host cell. Consequently, the principles of probe selection and array design can readily be extended to analyze more complex polymorphisms (see EP 730,663). For example, to characterize a triallelic SNP polymorphism, three groups of probes can be designed tiled on the three polymorphic forms as described above. As a further example, to analyze a diallelic polymorphism involving a deletion of a nucleotide, one can tile a first group of probes based on the undeleted polymorphic form as the reference sequence and a second group of probes based on the deleted form as the reference sequence.

For assay of genomic DNA, virtually any biological convenient tissue samples include whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin and hair can be used. Genomic DNA is typically amplified before analysis. Amplification is usually effected by PCR using primers flanking a suitable fragment e.g., of 50-500 nucleotides containing the locus of the polymorphism to be analyzed. Target is usually labeled in the course of amplification. The amplification product can be RNA or DNA, single stranded or double stranded. If double stranded, the amplification product is typically denatured before application to an array. If genomic DNA is analyzed without

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amplification, it may be desirable to remove RNA from the sample before applying it to the array. Such can be accomplished by digestion with DNase-free RNAase.

DETECTION OF POLYMORPHISMS IN A NUCLEIC ACID SAMPLE

The SNPs disclosed herein can be used to determine which forms of a characterized polymorphism are present in individuals under analysis.

The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki et al., Nature 324, 163-166 (1986); Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed that hybridize to a segment of target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in the respective segments from the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position (e.g., in a 15-mer at the 7 position; in a 16-mer, at either the 7, 8 or 9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

The polymorphisms can also be identified by hybridization to nucleic acid arrays, some examples of which are described in oublished PCT application WO 95/11995. WO 95/11995 also describes subarrays that are optimized for detection of a variant form of a precharacterized polymorphism. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first

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reference sequence. The second group of probes is designed by the same principles, except that the probes exhibit complementarity to the second reference sequence. The inclusion of a second group (or further groups) can be particularly useful for analyzing short subsequences of the primary reference sequence in which multiple mutations are expected to occur within a short distance commensurate with the length of the probes (e.g., two or more mutations within 9 to 21 bases).

An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism and only primes amplification of an allelic form to which the primer exhibits perfect complementarity. See Gibbs, Nucleic Acid Res. 17 2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two-primers, resulting in a detectable product which indicates the particular allelic form is present. A control is usually performed with a second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarity to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer (see, e.g., WO 93/22456).

Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent melting properties and electrophoretic migration of DNA in solution. Erlich, ed., PCR Technology, Principles and Applications for DNA Amplification, (W.H. Freeman and Co New York, 1992, Chapter 7).

Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita et al., Proc. Nat. Acad. Sci. 86, 2766-2770 (1989). Amplified PCR products can be generated and heated or otherwise denatured, to form single stranded amplification products. Single-

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stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence differences between alleles of target sequences.

The genotype of an individual with respect to a pathology suspected of being caused by a genetic polymorphism may be assessed by association analysis. Phenotypic traits suitable for association analysis include diseases that have known but hitherto unmapped genetic components (e.g., agammaglobulinemia, diabetes insipidus, Lesch-Nyhan syndrome, muscular dystrophy, Wiskott-Aldrich syndrome, Fabry's disease, familial hypercholesterolemia, polycystic kidney disease, hereditary spherocytosis, von Willebrand's disease, tuberous sclerosis, hereditary hemorrhagic telangiectasia, familial colonic polyposis, Ehlers-Danlos syndrome, osteogenesis imperfecta, and acute intermittent porphyria).

Phenotypic traits also include symptoms of, or susceptibility to, multifactorial diseases of which a component is or may be genetic, such as autoimmune diseases, inflammation, cancer, system, diseases of the nervous and infection by pathogenic microorganisms. Some examples of autoimmune diseases include rheumatoid arthritis, multiple sclerosis, diabetes (insulin-dependent and non- independent), systemic lupus erythematosus and Graves disease. Some examples of cancers include cancers of the bladder, brain, breast, colon, esophagus, kidney, oral cavity, ovary, pancreas, prostate, skin, stomach, leukemia, liver, lung, and uterus. Phenotypic traits also include characteristics such as longevity, appearance (e.g., baldness, obesity), strength, speed, endurance, fertility, and susceptibility or receptivity to particular drugs or therapeutic treatments.

Such correlations can be exploited in several ways. In the case of a strong correlation between a polymorphic form and a disease for which treatment is available, detection of the polymorphic form set in a human or animal patient may justify immediate administration of treatment, or at least the institution of regular monitoring of the patient. Detection of a polymorphic form correlated with serious disease in a couple

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contemplating a family may also be valuable to the couple in their reproductive decisions. For example, the female partner might elect to undergo in vitro fertilization to avoid the possibility of transmitting such a polymorphism from her husband to her offspring. In the case of a weaker, but still statistically significant correlation between a polymorphic set and human disease, immediate therapeutic intervention or monitoring may not be justified. Nevertheless, the patient can be motivated to begin simple life-style changes (e.g., diet, exercise) that can be accomplished at little cost to the patient but confer potential benefits in reducing the risk of conditions to which the patient may have increased susceptibility by virtue of variant alleles. After determining polymorphic form(s) present in an individual at one or more polymorphic sites, this information can be used in a number of methods.

Determination of which polymorphic forms occupy a set of polymorphic sites in an individual identifies a set of polymorphic forms that distinguishes the individual. See generally National Research Council, *The Evaluation of Forensic DNA Evidence* (Eds. Pollard et al., National Academy Press, DC, 1996). Since the polymorphic sites are within a 50,000 bp region in the human genome, the probability of recombination between these polymorphic sites is low. That low probability means the haplotype (the set of all 10 polymorphic sites) set forth in this application should be inherited without change for at least several generations. The more sites that are analyzed the lower the probability that the set of polymorphic forms in one individual is the same as that in an unrelated individual. Preferably, if multiple sites are analyzed, the sites are unlinked. Thus, polymorphisms of the invention are often used in conjunction with polymorphisms in distal genes. Preferred polymorphisms for use in forensics are diallelic because the population frequencies of two polymorphic forms can usually be determined with greater accuracy than those of multiple polymorphic forms at multi-allelic loci.

The capacity to identify a distinguishing or unique set of forensic markers in an individual is useful for forensic analysis. For example, one can determine whether a blood sample from a suspect matches a blood or other tissue sample from a crime scene by determining whether the set of polymorphic forms occupying selected polymorphic sites is the same in the suspect and the sample. If the set of polymorphic markers does not

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match between a suspect and a sample, it can be concluded (barring experimental error) that the suspect was not the source of the sample. If the set of markers does match, one can conclude that the DNA from the suspect is consistent with that found at the crime scene. If frequencies of the polymorphic forms at the loci tested have been determined (e.g., by analysis of a suitable population of individuals), one can perform a statistical analysis to determine the probability that a match of suspect and crime scene sample would occur by chance.

p(ID) is the probability that two random individuals have the same polymorphic or allelic form at a given polymorphic site. In diallelic loci, four genotypes are possible: AA, AB, BA, and BB. If alleles A and B occur in a haploid genome of the organism with frequencies x and y, the probability of each genotype in a diploid organism are (see WO 95/12607):

Homozygote:
$$p(AA)=x^2$$

Homozygote:
$$p(BB)=y^2=(1-x)^2$$

Single Heterozygote:
$$p(AB)=p(BA)=xy=x(1-x)$$

Both Heterozygotes:
$$p(AB+BA)=2xy=2x(1-x)$$

The probability of identity at one locus (i.e, the probability that two individuals, picked at random from a population will have identical polymorphic forms at a given locus) is given by the equation:

$$p(ID)=(x^2)^{2+}(2xy)^{2+}(y^2)^2$$
.

These calculations can be extended for any number of polymorphic forms at a given locus. For example, the probability of identity p(ID) for a 3-allele system where the alleles have the frequencies in the population of x, y and z, respectively, is equal to the sum of the squares of the genotype frequencies:

$$p(ID)=x^{4+}(2xy)^{2+}(2yz)^{2+}(2xz)^{2+}z^{4+}y^{4}$$

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In a locus of n alleles, the appropriate binomial expansion is used to calculate p(ID) and p(exc).

The cumulative probability of identity (cum p(ID)) for each of multiple unlinked loci is determined by multiplying the probabilities provided by each locus:

$$cum p(ID)=p(ID1)p(ID2)p(ID3) \dots p(IDn)$$

The cumulative probability of non-identity for n loci (i.e. the probability that two random individuals will be different at 1 or more loci) is given by the equation:

$$cum p(nonID)=1-cum p(ID).$$

If several polymorphic loci are tested, the cumulative probability of non-identity for random individuals becomes very high (e.g., one billion to one). Such probabilities can be taken into account together with other evidence in determining the guilt or innocence of the suspect.

The object of paternity testing is usually to determine whether a male is the father of a child. In most cases, the mother of the child is known and thus, the mother's contribution to the child's genotype can be traced. Paternity testing investigates whether the part of the child's genotype not attributable to the mother is consistent with that of the putative father. Paternity testing can be performed by analyzing sets of polymorphisms in the putative father and the child.

If the set of polymorphisms in the child attributable to the father does not match the putative father, it can be concluded, barring experimental error, that the putative father is not the real father. If the set of polymorphisms in the child attributable to the father does match the set of polymorphisms of the putative father, a statistical calculation can be performed to determine the probability of coincidental match.

The probability of parentage exclusion (representing the probability that a random male will have a polymorphic form at a given polymorphic site that makes him incompatible as the father) is given by the equation (see WO 95/12607):

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$$p(exc)=xy(1-xy)$$

where x and y are the population frequencies of alleles A and B of a diallelic polymorphic site. (At a triallelic site p(exc)=xy(1-xy)+yz(1-yz)+xz(1-xz)+3xyz(1-xyz)), where x, y and z and the respective population frequencies of alleles A, B and C). The probability of non-exclusion is:

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$$p(non-exc)=1-p(exc)$$

The cumulative probability of non-exclusion (representing the value obtained when n loci are used) is thus:

$$cum\ p(non-exc)=p(non-exc1)p(non-exc2)p(non-exc3)\dots p(non-excn)$$

The cumulative probability of exclusion for n loci (representing the probability that a random male will be excluded) is:

$$cum\ p(exc)=1-cum\ p(non-exc).$$

If several polymorphic loci are included in the analysis, the cumulative probability of exclusion of a random male is very high. This probability can be taken into account in assessing the liability of a putative father whose polymorphic marker set matches the child's polymorphic marker set attributable to his/her father.

The polymorphisms of the invention may contribute to the phenotype of an organism in different ways. Some polymorphisms occur within a protein coding sequence and contribute to phenotype by affecting protein structure. The effect may be neutral, beneficial or detrimental, or both beneficial and detrimental, depending on the circumstances. For example, a heterozygous sickle cell mutation confers resistance to malaria, but a homozygous sickle cell mutation is usually lethal. Other polymorphisms occur in noncoding regions but may exert phenotypic effects indirectly via influence on replication, transcription, and translation. A single polymorphism may affect more than one phenotypic trait. Likewise, a single phenotypic trait may be affected by polymorphisms in different genes. Further, some polymorphisms predispose an individual to a distinct mutation that is causally related to a certain phenotype.

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Phenotypic traits include diseases that have known but hitherto unmapped genetic components. Phenotypic traits also include symptoms of, or susceptibility to, multifactorial diseases of which a component is or may be genetic, such as autoimmune diseases, inflammation, cancer, diseases of the nervous system, and infection by pathogenic microorganisms. Some examples of autoimmune diseases include rheumatoid arthritis, multiple sclerosis, diabetes (insulin-dependent and non-independent), systemic lupus erythematosus and Graves disease. Some examples of cancers include cancers of the bladder, brain, breast, colon, esophagus, kidney, leukemia, liver, lung, oral cavity, ovary, pancreas, prostate, skin, stomach and uterus. Phenotypic traits also include characteristics such as longevity, appearance (e.g., baldness, obesity), strength, speed, endurance, fertility, and susceptibility or receptivity to particular drugs or therapeutic treatments.

Correlation is performed for a population of individuals who have been tested for the presence or absence of a phenotypic trait of interest and for polymorphic markers sets. To perform such analysis, the presence or absence of a set of polymorphisms (i.e. a polymorphic set) is determined for a set of the individuals, some of whom exhibit a particular trait, and some of which exhibit lack of the trait. The alleles of each polymorphism of the set are then reviewed to determine whether the presence or absence of a particular allele is associated with the trait of interest. Correlation can be performed by standard statistical methods such as a -squared test and statistically significant correlations between polymorphic form(s) and phenotypic characteristics are noted. For example, it might be found that the presence of allele A1 at polymorphism A correlates with heart disease. As a further example, it might be found that the combined presence of allele A1 at polymorphism A and allele B1 at polymorphism B correlates with increased milk production of a farm animal.

Such correlations can be exploited in several ways. In the case of a strong correlation between a set of one or more polymorphic forms and a disease for which treatment is available, detection of the polymorphic form set in a human or animal patient may justify immediate administration of treatment, or at least the institution of regular monitoring of the patient. Detection of a polymorphic form correlated with serious

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disease in a couple contemplating a family may also be valuable to the couple in their reproductive decisions. For example, the female partner might elect to undergo in vitro fertilization to avoid the possibility of transmitting such a polymorphism from her husband to her offspring. In the case of a weaker, but still statistically significant correlation between a polymorphic set and human disease, immediate therapeutic intervention or monitoring may not be justified. Nevertheless, the patient can be motivated to begin simple life-style changes (e.g., diet, exercise) that can be accomplished at little cost to the patient but confer potential benefits in reducing the risk of conditions to which the patient may have increased susceptibility by virtue of variant alleles. Identification of a polymorphic set in a patient correlated with enhanced receptiveness to one of several treatment regimes for a disease indicates that this treatment regime should be followed.

For animals and plants, correlations between characteristics and phenotype are useful for breeding for desired characteristics. For example, Beitz et al., U.S. Pat. No. 5,292,639 discuss use of bovine mitochondrial polymorphisms in a breeding program to improve milk production in cows. To evaluate the effect of mtDNA D-loop sequence polymorphism on milk production, each cow was assigned a value of 1 if variant or 0 if wild type with respect to a prototypical mitochondrial DNA sequence at each of 17 locations considered.

The previous section concerns identifying correlations between phenotypic traits and polymorphisms that directly or indirectly contribute to those traits. The present section describes identification of a physical linkage between a genetic locus associated with a trait of interest and polymorphic markers that are not associated with the trait, but are in physical proximity with the genetic locus responsible for the trait and co-segregate with it. Such analysis is useful for mapping a genetic locus associated with a phenotypic trait to a chromosomal position, and thereby cloning gene(s) responsible for the trait. See Lander et al., *Proc. Natl. Acad. Sci.* (USA) 83, 7353-7357 (1986); Lander et al., *Proc. Natl. Acad. Sci.* (USA) 84, 2363-2367 (1987); Donis-Keller et al., *Cell* 51, 319-337 (1987); Lander et al., *Genetics* 121, 185-199 (1989)). Genes localized by linkage can be cloned by a process known as directional cloning. See Wainwright, *Med. J. Australia*

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159, 170-174 (1993); Collins, *Nature Genetics* 1, 3-6 (1992) (each of which is incorporated by reference in its entirety for all purposes).

Linkage studies are typically performed on members of a family. Available members of the family are characterized for the presence or absence of a phenotypic trait and for a set of polymorphic markers. The distribution of polymorphic markers in an informative meiosis is then analyzed to determine which polymorphic markers cosegregate with a phenotypic trait. See, e.g., Kerem et al., *Science* 245, 1073-1080 (1989); Monaco et al., *Nature* 316, 842 (1985); Yamoka et al., *Neurology* 40, 222-226 (1990); Rossiter et al., *FASEB Journal* 5, 21-27 (1991).

Linkage is analyzed by calculation of LOD (log of the odds) values. A lod value is the relative likelihood of obtaining observed segregation data for a marker and a genetic locus when the two are located at a recombination fraction , versus the situation in which the two are not linked, and thus segregating independently (Thompson & Thompson, Genetics in Medicine (5th ed, W.B. Saunders Company, Philadelphia, 1991); Strachan, "Mapping the human genome" in The Human Genome (BIOS Scientific Publishers Ltd, Oxford), Chapter 4). A series of likelihood ratios are calculated at various =0.0 (coincident loci) to =0.50recombination fractions (), ranging from is: probability of data if loci (unlinked). Thus, the likelihood at a given value of to probability of data if loci unlinked. The computed likelihood is usually linked at expressed as the log₁₀ of this ratio (i.e., a lod score). For example, a lod score of 3 indicates 1000:1 odds against an apparent observed linkage being a coincidence. The use of logarithms allows data collected from different families to be combined by simple addition. Computer programs are available for the calculation of lod scores for differing (e.g., LIPED, MLINK (Lathrop, Proc. Nat. Acad. Sci. (USA) 81, 3443values of 3446 (1984)). For any particular lod score, a recombination fraction may be determined from mathematical tables. See Smith et al., Mathematical tables for research workers in human genetics (Churchill, London, 1961); Smith, Ann. Hum. Genet. 32, 127-150 (1968). at which thelod score is the highest is considered to be the best The value of estimate of the recombination fraction.

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Positive lod score values suggest that the two loci are linked, whereas negative values suggest that linkage is less likely (at that value of) than the possibility that the two loci are unlinked. By convention, a combined lod score of + 3 or greater (equivalent to greater than 1000:1 odds in favor of linkage) is considered definitive evidence that two loci are linked. Similarly, by convention, a negative lod score of -2 or less is taken as definitive evidence against linkage of the two loci being compared. Negative linkage data are useful in excluding a chromosome or a segment thereof from consideration. The search focuses on the remaining non-excluded chromosomal locations.

The invention further provides transgenic nonhuman animals capable of expressing an exogenous variant gene and/or having one or both alleles of an endogenous variant gene inactivated. Expression of an exogenous variant gene is usually achieved by operably linking the gene to a promoter and optionally an enhancer, and microinjecting the construct into a zygote. See Hogan et al., "Manipulating the Mouse Embryo, A Laboratory Manual," Cold Spring Harbor Laboratory. (1989). Inactivation of endogenous variant genes can be achieved by forming a transgene in which a cloned variant gene is inactivated by insertion of a positive selection marker. See Capecchi, Science 244, 1288-1292 The transgene is then introduced into an embryonic stem cell, where it undergoes homologous recombination with an endogenous variant gene. Mice and other rodents are preferred animals. Such animals provide useful drug screening systems.

The invention further provides methods for assessing the pharmacogenomic susceptibility of a subject harboring a single nucleotide polymorphism to a particular pharmaceutical compound, or to a class of such compounds. Genetic polymorphism in drug-metabolizing enzymes, drug transporters, receptors for pharmaceutical agents, and other drug targets have been correlated with individual differences based on distinction in the efficacy and toxicity of the pharmaceutical agent administered to a subject. Pharmocogenomic characterization of a subjects susceptibility to a drug enhances the ability to tailor a dosing regimen to the particular genetic constitution of the subject, thereby enhancing and optimizing the therapeutic effectiveness of the therapy.

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In cases in which a cSNP leads to a polymorphic protein that is ascribed to be the cause of a pathological condition, method of treating such a condition includes administering to a subject experiencing the pathology the wild type cognate of the polymorphic protein. Once administered in an effective dosing regimen, the wild type cognate provides complementation or remediation of the defect due to the polymorphic protein. The subject's condition is ameliorated by this protein therapy.

A subject suspected of suffering from a pathology ascribable to a polymorphic protein that arises from a cSNP is to be diagnosed using any of a variety of diagnostic methods capable of identifying the presence of the cSNP in the nucleic acid, or of the cognate polymorphic protein, in a suitable clinical sample taken from the subject. Once the presence of the cSNP has been ascertained, and the pathology is correctable by administering a normal or wild-type gene, the subject is treated with a pharmaceutical composition that includes a nucleic acid that harbors the correcting wild-type gene, or a fragment containing a correcting sequence of the wild-type gene. Non-limiting examples of ways in which such a nucleic acid may be administered include incorporating the wildtype gene in a viral vector, such as an adenovirus or adeno associated virus, and administration of a naked DNA in a pharmaceutical composition that promotes intracellular uptake of the administered nucleic acid. Once the nucleic acid that includes the gene coding for the wild-type allele of the polymorphism is incorporated within a cell of the subject, it will initiate de novo biosynthesis of the wild-type gene product. If the nucleic acid is further incorporated into the genome of the subject, the treatment will have long-term effects, providing de novo synthesis of the wild-type protein for a prolonged duration. The synthesis of the wild-type protein in the cells of the subject will contribute to a therapeutic enhancement of the clinical condition of the subject.

A subject suffering from a pathology ascribed to a SNP may be treated so as to correct the genetic defect. (See Kren et al., Proc. Natl. Acad. Sci. USA 96:10349-10354 (1999)). Such a subject is identified by any method that can detect the polymorphism in a sample drawn from the subject. Such a genetic defect may be permanently corrected by administering to such a subject a nucleic acid fragment incorporating a repair sequence that supplies the wild-type nucleotide at the position of the SNP. This site-specific repair

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sequence encompasses an RNA/DNA oligonucleotide which operates to promote endogenous repair of a subject's genomic DNA. Upon administration in an appropriate vehicle, such as a complex with polyethylenimine or encapsulated in anionic liposomes, a genetic defect leading to an inborn pathology may be overcome, as the chimeric oligonucleotides induces incorporation of the wild-type sequence into the subject's genome. Upon incorporation, the wild-type gene product is expressed, and the replacement is propagated, thereby engendering a permanent repair.

The invention further provides kits comprising at least one allele-specific oligonucleotide as described above. Often, the kits contain one or more pairs of allele-specific oligonucleotides hybridizing to different forms of a polymorphism. In some kits, the allele-specific oligonucleotides are provided immobilized to a substrate. For example, the same substrate can comprise allele-specific oligonucleotide probes for detecting at least 10, 100, 1000 or all of the polymorphisms shown in the Table. Optional additional components of the kit include, for example, restriction enzymes, reverse-transcriptase or polymerase, the substrate nucleoside triphosphates, means used to label (for example, an avidin-enzyme conjugate and enzyme substrate and chromogen if the label is biotin), and the appropriate buffers for reverse transcription, PCR, or hybridization reactions. Usually, the kit also contains instructions for carrying out the hybridizing methods.

Several aspects of the present invention rely on having available the polymorphic proteins encoded by the nucleic acids comprising a SNP of the inventions. There are various methods of isolating these nucleic acid sequences. For example, DNA is isolated from a genomic or cDNA library using labeled oligonucleotide probes having sequences complementary to the sequences disclosed herein.

Such probes can be used directly in hybridization assays. Alternatively probes can be designed for use in amplification techniques such as PCR.

To prepare a cDNA library, mRNA is isolated from tissue such as heart or pancreas, preferably a tissue wherein expression of the gene or gene family is likely to occur. cDNA is prepared from the mRNA and ligated into a recombinant vector. The

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vector is transfected into a recombinant host for propagation, screening and cloning.

Methods for making and screening cDNA libraries are well known, See Gubler, U. and Hoffman, B.J. Gene 25:263-269 (1983) and Sambrook et al.

For a genomic library, for example, the DNA is extracted from tissue and either mechanically sheared or enzymatically digested to yield fragments of about 12-20 kb. The fragments are then separated by gradient centrifugation from undesired sizes and are constructed in bacteriophage lambda vectors. These vectors and phage are packaged *in vitro*, as described in Sambrook, et al. Recombinant phage are analyzed by plaque hybridization as described in Benton and Davis, <u>Science</u> 196:180-1 82 (1977). Colony hybridization is carried out as generally described in M. Grunstein et al. Proc. Natl. Acad. Sci. USA. 72:3961-3965 (1975). DNA of interest is identified in either cDNA or genomic libraries by its ability to hybridize with nucleic acid probes, for example on Southern blots, and these DNA regions are isolated by standard methods familiar to those of skill in the art. See Sambrook, et al.

In PCR techniques, oligonucleotide primers complementary to the two 3' borders of the DNA region to be amplified are synthesized. The polymerase chain reaction is then carried out using the two primers. See PCR Protocols: a Guide to Methods and Applications (Innis, M, Gelfand, D., Sninsky, J. and White, T., eds.), Academic Press, San Diego (1990). Primers can be selected to amplify the entire regions encoding a full-length sequence of interest or to amplify smaller DNA. segments as desired. PCR can be used in a variety of protocols to isolate cDNA's encoding a sequence of interest. In these protocols, appropriate primers and probes for amplifying DNA encoding a sequence of interest are generated from analysis of the DNA sequences listed herein. Once such regions are PCR-amplified, they can be sequenced and oligonucleotide probes can be prepared from the sequence.

Once DNA encoding a sequence comprising a cSNP is isolated and cloned, one can express the encoded polymorphic proteins in a variety of recombinantly engineered cells. It is expected that those of skill in the art are knowledgeable in the numerous expression systems available for expression of DNA encoding a sequence of interest. No

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attempt to describe in detail the various methods known for the expression of proteins in prokaryotes or eukaryotes is made here.

In brief summary, the expression of natural or synthetic nucleic acids encoding a sequence of interest will typically be achieved by operably linking the DNA or cDNA to a promoter (which is either constitutive or inducible), followed by incorporation into an expression vector. The vectors can be suitable for replication and integration in either prokaryotes or eukaryotes. Typical expression vectors contain, initiation sequences, transcription and translation terminators, and promoters useful for regulation of the expression of a polynucleotide sequence of interest. To obtain high level expression of a cloned gene, it is desirable to construct expression plasmids which contain, at the minimum, a strong promoter to direct transcription, a ribosome binding site for translational initiation, and a transcription/translation terminator. The expression vectors may also comprise generic expression cassettes containing at least one independent terminator sequence, sequences permitting replication of the plasmid in both eukaryotes and prokaryotes, i.e., shuttle vectors, and selection markers for both prokaryotic and eukaryotic systems. See Sambrook et al.

A variety of prokaryotic expression systems may be used to express the polymorphic proteins of the invention. Examples include *E. coli*, Bacillus, Streptomyces, and the like.

It is preferred to construct expression plasmids which contain, at the minimum, a strong promoter to direct transcription, a ribosome binding site for translational initiation, and a transcription/translation terminator. Examples of regulatory regions suitable for this purpose in *E. coli* are the promoter and operator region of the *E. coli* tryptophan biosynthetic pathway as described by Yanofsky, C., J. Bacterial. 158:1018-1024 (1984) and the leftward promoter of phage lambda (P) as described by Λ, I. and Hagen, D., Ann. Rev. Genet. 14:399-445 (1980). The inclusion of selection markers in DNA vectors transformed in *E. coli* is also useful. Examples of such markers include genes specifying resistance to ampicillin, tetracycline, or chloramphenicol. See Sambrook et al. for details concerning selection markers for use in *E. coli*.

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To enhance proper folding of the expressed recombinant protein, during purification from *E. coli*, the expressed protein may first be denatured and then renatured. This can be accomplished by solubilizing the bacterially produced proteins in a chaotropic agent such as guanidine HCI and reducing all the cysteine residues with a reducing agent such as beta-mercaptoethanol. The protein is then renatured, either by slow dialysis or by gel filtration. See U.S. Patent No. 4,511,503. Detection of the expressed antigen is achieved by methods known in the art as radioimmunoassay, or Western blotting techniques or immunoprecipitation. Purification from *E. coli* can be achieved following procedures such as those described in U.S. Patent No. 4,511,503.

Any of a variety of eukaryotic expression systems such as yeast, insect cell lines, bird, fish, and mammalian cells, may also be used to express a polymorphic protein of the invention. As explained briefly below, a nucleotide sequence harboring a cSNP may be expressed in these eukaryotic systems. Synthesis of heterologous proteins in yeast is well known. Methods in Yeast Genetics, Sherman, F., et al., Cold Spring Harbor Laboratory, (1982) is a well recognized work describing the various methods available to produce the protein in yeast. Suitable vectors usually have expression control sequences, such as promoters, including 3-phosphogtycerate kinase or other glycolytic enzymes, and an origin of replication, termination sequences and the like as desired. For instance, suitable vectors are described in the literature (Botstein, et al., Gene 8:17-24 (1979); Broach, et al., Gene 8:121-133 (1979)).

Two procedures are used in transforming yeast cells. In one case, yeast cells are first converted into protoplasts using zymolyase, lyticase or glusulase, followed by addition of DNA and polyethylene glycol (PEG). The PEG-treated protoplasts are then regenerated in a 3% agar medium under selective conditions. Details of this procedure are given in the papers by J.D. Beggs, Nature (London) 275:104-109 (1978); and Hinnen, A., et al., Proc. Natl. Acad. Sci. USA, 75:1929-1933 (1978). The second procedure does not involve removal of the cell wall. Instead the cells are treated with lithium chloride or acetate and PEG and put on selective plates (Ito, H., et al., J. Bact, 153163-168 (1983)). cells and applying standard protein isolation techniques to the lysates:.

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The purification process can be monitored by using Western blot techniques or radioimmunoassay or other standard techniques. The sequences encoding the proteins of the invention can also be ligated to various immunoassay expression vectors for use in transforming cell cultures of, for instance, mammalian, insect, bird or fish origin.

Illustrative of cell cultures useful for the production of the polypeptides are mammalian cells. Mammalian cell systems often will be in the form of monolayers of cells although mammalian cell suspensions may also be used. A number of suitable host cell lines capable of expressing intact proteins have been developed in the art, and include the HEK293, BHK21, and CHO cell lines, and various human cells such as COS cell lines, HeLa cells, myeloma cell lines, Jurkat cells, etc. Expression vectors for these cells can include expression control sequences, such as an origin of replication, a promoter (e.g., the CMV promoter, a HSV *tk* promoter or *pgk* (phosphoglycerate kinase) promoter), an enhancer (Queen et al. Immunol. Rev. 89:49 (1986)) and necessary processing information sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites (e.g., an SV40 large T Ag poly A addition site), and transcriptional terminator sequences.

Other animal cells are available, for instance, from the American Type Culture Collection Catalogue of Cell Lines and Hybridomas (7th edition, (1992)). Appropriate vectors for expressing the proteins of the invention in insect cells are usually derived from baculovirus. Insect cell lines include mosquito larvae, silkworm, armyworm, moth and Drosophila cell lines such as a Schneider cell line (See Schneider J. Embryol. Exp. Morphol., 27:353-365 (1987). As indicated above, the vector, e.g., a plasmid, which is used to transform the host cell, preferably contains DNA sequences to initiate transcription and sequences to control the translation of the protein. These sequences are referred to as expression control sequences. As with yeast, when higher animal host cells are employed, polyadenylation or transcription terminator sequences from known mammalian genes need to be incorporated into the vector. An example of a terminator sequence is the polyadenylation sequence from the bovine growth hormone gene. Sequences for accurate splicing of the transcript may also be included. An example of a splicing sequence is the VP1 intron from SV4O (Sprague, J. et a/., J. Virol. 45: 773-781 (1983)). Additionally, gene sequences to control replication in the host cell may be Saveria-Campo, M., 1985, "Bovine Papilloma virus DNA a Eukaryotic Cloning Vector"

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in DNA Cloning Vol. II a Practical Approach Ed. D.M. Glover, IRL Press, Arlington, Virginia pp. 213-238. The host cells are competent or rendered competent for transformation by various means. There are several well-known methods of introducing DNA into animal cells. These include: calcium phosphate precipitation, fusion of the recipient cells with bacterial protoplasts containing the DNA, treatment of the recipient cells with liposomes containing the DNA, DEAE dextran, electroporation and microinjection of the DNA directly into the cells.

The transformed cells are cultured by means well known in the art (Biochemical Methods in Cell Culture and Virology, Kuchler, R.J., Dowden, Hutchinson and Ross, Inc., (1977)). The expressed polypeptides are isolated from cells grown as suspensions or as monolayers. The latter are recovered by well known mechanical, chemical or enzymatic means.

General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, Methods in Enzymology 185, 537-566 (1990). As defined herein "operably linked" refers to linkage of a promoter upstream from a DNA sequence such that the promoter mediates transcription of the DNA sequence. Specifically, "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the gene encoding the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression sequence. The term "vector", refers to viral expression systems, autonomous self-replicating circular DNA (plasmids), and includes both expression and nonexpression plasmids.

The term "gene" as used herein is intended to refer to a nucleic acid sequence which encodes a polypeptide. This definition includes various sequence polymorphisms, mutations, and/or sequence variants wherein such alterations do not affect the function of the gene product. The term "gene" is intended to include not only coding sequences but also regulatory regions such as promoters, enhancers, termination regions and similar untranslated nucleotide sequences. The term further includes all introns and other DNA sequences spliced from the mRNA transcript, along with variants resulting from

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5 alternative splice sites.

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A43 1 cells, human Co10205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from in vitro culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL- 60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include Saccharomyces cerevisiae. Schizosaccharomyces pombe, Kluyveromyces strains, Candida or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include Escherichia coli, Bacillus subtilis, Salmonella typhimurium, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, California, U.S.A. (the MaxBac© kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed." The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein.

The polymorphic protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide

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sequence encoding the protein. The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are known to those skilled in the art.

The polymorphic proteins produced by recombinant DNA technology may be purified by techniques commonly employed to isolate or purify recombinant proteins. Recombinantly produced proteins can be directly expressed or expressed as a fusion protein. The protein is then purified by a combination of cell lysis (e.g., sonication) and affinity chromatography. For fusion products, subsequent digestion of the fusion protein with an appropriate proteolytic enzyme releases the desired polypeptide. The polypeptides of this invention may be purified to substantial purity by standard techniques well known in the art, including selective precipitation with such substances as ammonium sulfate, column chromatography, immunopurification methods, and others. See, for instance, R. Scopes, Protein Purification: Principles and Practice, Springer-Verlag: New York (1982), incorporated herein by reference. For example, in an embodiment, antibodies may be raised to the proteins of the invention as described herein. Cell membranes are isolated from a cell line expressing the recombinant protein, the protein is extracted from the membranes and immunoprecipitated. The proteins may then be further purified by standard protein chemistry techniques as described above.

The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-Toyopearl@ or Cibacrom blue 3GA Sepharose B; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography. Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, MA),

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Pharmacia (Piscataway, NJ) and InVitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("Flag") is commercially available from Kodak (New Haven, CT). Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, *i.e.*, molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen, such as polymorphic. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab} and $F_{(ab')2}$ fragments, and an F_{ab} expression library. In a specific embodiment, antibodies to human polymorphic proteins are disclosed.

The phrase "specifically binds to", "immunospecifically binds to" or is "specifically immunoreactive with", an antibody when referring to a protein or peptide, refers to a binding reaction which is determinative of the presence of the protein in the presence of a heterogeneous population of proteins and other biological materials. Thus, for example, under designated immunoassay conditions, the specified antibodies bind to a particular protein and do not bind in a significant amount to other proteins present in the sample. Specific binding to an antibody under such conditions may require an antibody that is selected for its specificity for a particular protein. Of particular interest in the present invention is an antibody that binds immunospecifically to a polymorphic protein but not to its cognate wild type allelic protein, or vice versa. A variety of immunoassay formats may be used to select antibodies specifically immunoreactive with a particular protein. For example, solid-phase ELISA immunoassays are routinely used to select monoclonal antibodies specifically immunoreactive with a protein. See Harlow and Lane

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5 (1988) Antibodies, a Laboratory Manual, Cold Spring Harbor Publications, New York, for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity.

Polyclonal and/or monoclonal antibodies that immunospecifically bind to polymorphic gene products but not to the corresponding prototypical or "wild-type" gene products are also provided. Antibodies can be made by injecting mice or other animals with the variant gene product or synthetic peptide. Monoclonal antibodies are screened as are described, for example, in Harlow & Lane, Antibodies, A Laboratory Manual, Cold Spring Harbor Press, New York (1988); Goding, Monoclonal antibodies, Principles and Practice (2d ed.) Academic Press, New York (1986). Monoclonal antibodies are tested for specific immunoreactivity with a variant gene product and lack of immunoreactivity to the corresponding prototypical gene product.

An isolated polymorphic protein, or a portion or fragment thereof, can be used as an immunogen to generate the antibody that bind the polymorphic protein using standard techniques for polyclonal and monoclonal antibody preparation. The full-length polymorphic protein can be used or, alternatively, the invention provides antigenic peptide fragments of polymorphic for use as immunogens. The antigenic peptide of a polymorphic protein of the invention comprises at least 8 amino acid residues of the amino acid sequence encompassing the polymorphic amino acid and encompasses an epitope of the polymorphic protein such that an antibody raised against the peptide forms a specific immune complex with the polymorphic protein. Preferably, the antigenic peptide comprises at least 10 amino acid residues, more preferably at least 15 amino acid residues, even more preferably at least 20 amino acid residues, and most preferably at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of polymorphic that are located on the surface of the protein, *e.g.*, hydrophilic regions.

For the production of polyclonal antibodies, various suitable host animals (e.g., rabbit, goat, mouse or other mammal) may be immunized by injection with the polymorphic protein. An appropriate immunogenic preparation can contain, for example,

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recombinantly expressed polymorphic protein or a chemically synthesized polymorphic polypeptide. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), human adjuvants such as *Bacille Calmette-Guerin* and *Corynebacterium parvum*, or similar immunostimulatory agents. If desired, the antibody molecules directed against polymorphic proteins can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as protein A chromatography, to obtain the IgG fraction.

The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that originates from the clone of a singly hybridoma cell, and that contains only one type of antigen binding site capable of immunoreacting with a particular epitope of a polymorphic protein. A monoclonal antibody composition thus typically displays a single binding affinity for a particular polymorphic protein with which it immunoreacts. For preparation of monoclonal antibodies directed towards a particular polymorphic protein, or derivatives, fragments, analogs or homologs thereof, any technique that provides for the production of antibody molecules by continuous cell line culture may be utilized. Such techniques include, but are not limited to, the hybridoma technique (see Kohler & Milstein, 1975 Nature 256: 495-497); the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to a polymorphic protein (see *e.g.*, U.S. Patent No.

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4,946,778). In addition, methodologies can be adapted for the construction of F_{ab} expression libraries (see *e.g.*, Huse, *et al.*, 1989 *Science* 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a polymorphic protein or derivatives, fragments, analogs or homologs thereof. Non-human antibodies can be "humanized" by techniques well known in the art. See *e.g.*, U.S. Patent No. 5,225,539. Antibody fragments that contain the idiotypes to a polymorphic protein may be produced by techniques known in the art including, but not limited to: (*i*) an F_{(ab')2} fragment produced by pepsin digestion of an antibody molecule; (*ii*) an F_{ab} fragment generated by reducing the disulfide bridges of an F_{(ab')2} fragment; (*iii*) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (*iv*) F_v fragments.

Additionally, recombinant anti-polymorphic protein antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in PCT International Application No. PCT/US86/02269; European Patent Application No. 184,187; European Patent Application No. 171,496; European Patent Application No. 173,494; PCT International Publication No. WO 86/01533; U.S. Pat. No. 4,816,567; European Patent Application No. 125,023; Better et al. (1988) Science 240:1041-1043; Liu et al. (1987) PNAS 84:3439-3443; Liu et al. (1987) J Immunol. 139:3521-3526; Sun et al. (1987) PNAS 84:214-218; Nishimura et al. (1987) Cancer Res 47:999-1005; Wood et al. (1985) Nature 314:446-449; Shaw et al. (1988) J Natl Cancer Inst 80:1553-1559); Morrison(1985) Science 229:1202-1207; Oi et al. (1986) BioTechniques 4:214; U.S. Pat. No. 5,225,539; Jones et al. (1986) Nature 321:552-525; Verhoeyan et al. (1988) Science 239:1534; and Beidler et al. (1988) J Immunol 141:4053-4060.

In one embodiment, methodologies for the screening of antibodies that possess the desired specificity include, but are not limited to, enzyme-linked immunosorbent assay (ELISA) and other immunologically-mediated techniques known within the art.

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Anti-polymorphic protein antibodies may be used in methods known within the art relating to the detection, quantitation and/or cellular or tissue localization of a polymorphic protein (e.g., for use in measuring levels of the polymorphic protein within appropriate physiological samples, for use in diagnostic methods, for use in imaging the protein, and the like). In a given embodiment, antibodies for polymorphic proteins, or derivatives, fragments, analogs or homologs thereof, that contain the antibody-derived CDR, are utilized as pharmacologically-active compounds in therapeutic applications intended to treat a pathology in a subject that arises from the presence of the cSNP allele in the subject.

An anti-polymorphic protein antibody (e.g., monoclonal antibody) can be used to isolate polymorphic proteins by a variety of immunochemical techniques, such as immunoaffinity chromatography or immunoprecipitation. An anti-polymorphic protein antibody can facilitate the purification of natural polymorphic protein from cells and of recombinantly produced polymorphic proteins expressed in host cells. Moreover, an anti-polymorphic protein antibody can be used to detect polymorphic protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the polymorphic protein. Anti-polymorphic antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ¹²⁵I, ¹³¹I, ³⁵S or ³H.

WHAT IS CLAIMED IS:

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- 1. An isolated polynucleotide selected from the group consisting of:
 - a) a nucleotide sequence comprising one or more polymorphic sequences (SEQ ID NOS:1 651);
 - b) a fragment of said nucleotide sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence;
 - c) a complementary nucleotide sequence comprising a sequence complementary to one or more of said polymorphic sequences (SEQ ID NOS:1 - 651); and
 - d) a fragment of said complementary nucleotide sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence.
- 2. The polynucleotide of claim 1, wherein said polynucleotide sequence is DNA.
- 20 3. The polynucleotide of claim 1, wherein said polynucleotide sequence is RNA.
 - 4. The polynucleotide of claim 1, wherein said polynucleotide sequence is between about 10 and about 100 nucleotides in length.
- 25 5. The polynucleotide of claim 1, wherein said polynucleotide sequence is between about 10 and about 90 nucleotides in length.

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6. The polynucleotide of claim 1, wherein said polynucleotide sequence is between about 10 and about 75 nucleotides in length.

7. The polynucleotide of claim 1, wherein said polynucleotide is between about 10 and about 50 bases in length.

8. The polynucleotide of claim 1, wherein said polynucleotide is between about 10 and about 40 bases in length.

15 9. The polynucleotide of claim 1, wherein said polynucleotide is derived from a nucleic acid encoding a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

20 10. The polynucleotide of claim 1, wherein said polymorphic site includes a nucleotide other than the nucleotide listed in Table 1, column 5 for said polymorphic sequence.

11. The polynucleotide of claim 1, wherein the complement of said polymorphic site includes a nucleotide other than the complement of the nucleotide listed in Table 1, column 5 for the complement of said polymorphic sequence.

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- The polynucleotide of claim 1, wherein said polymorphic site includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence.
 - 13. The polynucleotide of claim 1, wherein the complement of said polymorphic site includes the complement of the nucleotide listed in Table 1, column 6 for said polymorphic sequence.
 - 14. An isolated allele-specific oligonucleotide that hybridizes to a first polynucleotide at a polymorphic site encompassed therein, wherein the first polynucleotide is chosen from the group consisting of:
 - a) a nucleotide sequence comprising one or more polymorphic sequences
 (SEQ ID NOS:1 651) provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence;
 - b) a nucleotide sequence that is a fragment of said polymorphic sequence,
 provided that the fragment includes a polymorphic site in said
 polymorphic sequence;
 - c) a complementary nucleotide sequence comprising a sequence complementary to one or more polymorphic sequences (SEQ ID NOS:1 651), provided that the complementary nucleotide sequence includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5; and
 - d) a nucleotide sequence that is a fragment of said complementary sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence.

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- The oligonucleotide of claim 14, wherein the oligonucleotide does not hybridize under stringent conditions to a second polynucleotide selected from the group consisting of:
 - a) a nucleotide sequence comprising one or more polymorphic sequences
 (SEQ ID NOS:1 651), wherein said polymorphic sequence includes
 the nucleotide listed in Table 1, column 5 for said polymorphic
 sequence;
 - b) a nucleotide sequence that is a fragment of any of said nucleotide sequences;
 - c) a complementary nucleotide sequence comprising a sequence
 complementary to one or more polymorphic sequences (SEQ ID NOS:1
 651), wherein said polymorphic sequence includes the complement of
 the nucleotide listed in Table 1, column 5; and
 - d) a nucleotide sequence that is a fragment of said complementary sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence.
 - 16. The oligonucleotide of claim 15, wherein the oligonucleotide is between about 10 and about 51 bases in length.
- The oligonucleotide of claim 15, wherein the oligonucleotide identifies a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

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- 5 18. The oligonucleotide of claim 15, wherein the oligonucleotide is between about 15 and about 30 bases in length.
 - 19. A method of detecting a polymorphic site in a nucleic acid, the method comprising:
 - a) contacting said nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected from the group consisting of SEQ ID NOS: 1 651, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5; and
 - b) determining whether said nucleic acid and said oligonucleotide hybridize;

whereby hybridization of said oligonucleotide to said nucleic acid sequence indicates the presence of the polymorphic site in said nucleic acid.

- 20. The method of claim 19, wherein said oligonucleotide does not hybridize to said polymorphic sequence when said polymorphic sequence includes the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or when the complement of the polymorphic sequence includes the complement of the nucleotide recited in Table 1, column 5 for said polymorphic sequence.
- 21. The method of claim 19, wherein said oligonucleotide identifies a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

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- 22. The method of claim 19, wherein said oligonucleotide is between about 15 and about 30 bases in length.
- 23. A method of detecting the presence of a sequence polymorphism in a subject, the method comprising:
 - a) providing a nucleic acid from said subject;
 - b) contacting said nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 651, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5; and
 - c) determining whether said nucleic acid and said oligonucleotide hybridize;

whereby hybridization of said oligonucleotide to said nucleic acid sequence indicates the presence of the polymorphism in said subject.

- 24. A method of determining the relatedness of a first and second nucleic acid, the method comprising:
 - a) providing a first nucleic acid and a second nucleic acid;
 - b) contacting said first nucleic acid and said second nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement,

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provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5;

- c) determining whether said first nucleic acid and said second nucleic acid hybridize to said oligonucleotide; and
- d) comparing hybridization of said first and second nucleic acids to said oligonucleotide,

wherein hybridization of the first and second nucleic acids to said oligonucleotide indicates the first and second nucleic acids are related.

- 25. The method of claim 24, wherein said oligonucleotide does not hybridize to said polymorphic sequence when said polymorphic sequence includes the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or when the complement of the polymorphic sequence includes the complement of the nucleotide recited in Table 1, column 5 for said polymorphic sequence.
- 26. The method of claim 24, wherein the oligonucleotide is between about 10 and about 51 bases in length.
- 25 27. The method of claim 24, wherein the oligonucleotide is between about 10 and about 40 bases in length.
 - 28. The method of claim 24, wherein the oligonucleotide is between about 15 and about 30 bases in length.

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- An isolated polypeptide comprising a polymorphic site at one or more amino acid residues, wherein the protein is encoded by a polynucleotide selected from the group consisting of: polymorphic sequences SEQ ID NOS:1 651, or their complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5.
 - 30. The polypeptide of claim 29, wherein said polypeptide is translated in the same open reading frame as is a wild type protein whose amino acid sequence is identical to the amino acid sequence of the polymorphic protein except at the site of the polymorphism.
 - 31. The polypeptide of claim 29, wherein the polypeptide encoded by said polymorphic sequence, or its complement, includes the nucleotide listed in Table 2, column 6 or Table 3, column 5 for said polymorphic sequence, or the complement includes the complement of the nucleotide listed in Table 1, column 6.
- 32. An antibody that binds specifically to a polypeptide encoded by a polynucleotide comprising a nucleotide sequence encoded by a polynucleotide selected from the group consisting of polymorphic sequences SEQ ID NOS:1 651, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5.

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- 5 33. The antibody of claim 32, wherein said antibody binds specifically to a polypeptide encoded by a polymorphic sequence which includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence.
- The antibody of claim 32, wherein said antibody does not bind specifically to a polypeptide encoded by a polymorphic sequence which includes the nucleotide listed in Table 1, column 5 for said polymorphic sequence.
 - 35. A method of detecting the presence of a polypeptide having one or more amino acid residue polymorphisms in a subject, the method comprising
 - a) providing a protein sample from said subject;
 - b) contacting said sample with the antibody of claim 34 under conditions that allow for the formation of antibody-antigen complexes; and
 - c) detecting said antibody-antigen complexes,

whereby the presence of said complexes indicates the presence of said polypeptide.

- 36. A method of treating a subject suffering from, at risk for, or suspected of, suffering from a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:
- a) providing a subject suffering from a pathology associated with aberrant expression of a first nucleic acid comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 651, or its complement; and

b) administering to the subject an effective therapeutic dose of a second nucleic acid comprising the polymorphic sequence, provided that the second nucleic acid comprises the nucleotide present in a wild type allele of the sequence polymorphism,

thereby treating said subject.

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37. The method of claim 36, wherein the second nucleic acid sequence comprises a polymorphic sequence which includes the nucleotide listed in Table 1, column 5 for said polymorphic sequence.

Figure 1 15

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A method of treating a subject suffering from, at risk for, or suspected of suffering from a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:

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- a) providing a subject suffering from a pathology associated with aberrant expression of a polymorphic sequence selected from the group consisting of polymorphic sequences SEQ ID NOS:1 - 651, or its complement; and
- b) administering to the subject an effective therapeutic dose of a polypeptide,

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wherein said polypeptide is encoded by a polynucleotide comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or by a polynucleotide comprising a nucleotide sequence that is complementary to any one of polymorphic sequences SEQ ID NOS:1 - 651, provided that said polymorphic sequence includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence, thereby treating said subject.

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- 5 39. A method of treating a subject suffering from, at risk for, or suspected of suffering from, a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:
 - a) providing a subject suffering from, at risk for, or suspected of suffering from, a pathology associated with aberrant expression of a first nucleic acid comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 651, or its complement; and
 - b) administering to the subject an effective dose of the antibody of claim 34,

thereby treating said subject.

- 40. A method of treating a subject suffering from, at risk for, or suspected of suffering from, a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:
 - a) providing a subject suffering from, at risk for, or suspected of suffering from, a pathology associated with aberrant expression of a nucleic acid comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement; and
 - b) administering to the subject an effective dose of an oligonucleotide comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or by a polynucleotide comprising a nucleotide sequence that is complementary to any one of polymorphic sequences SEQ ID NOS:1 - 651, provided that said polymorphic sequence includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence,
- 30 thereby treating said subject.

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- 41. An oligonucleotide array, comprising one or more oligonucleotides hybridizing to a first polynucleotide at a polymorphic site encompassed therein, wherein the first polynucleotide is chosen from the group consisting of:
 - a) a nucleotide sequence comprising one or more polymorphic sequences SEQ ID NOS:1 651;
 - b) a nucleotide sequence that is a fragment of any of said nucleotide sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence;
 - c) a complementary nucleotide sequence comprising a sequence complementary to one or more polymorphic sequences SEQ ID NOS:1 - 651; and
 - d) a nucleotide sequence that is a fragment of said complementary sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence.

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- 42. The array of claim 41, wherein said array comprises 10 oligonucleotides.
- 43. The array of claim 41, wherein said array comprises at least 100 oligonucleotides.
- 25 44. The array of claim 41, wherein said array comprises at least 1000 oligonucleotides.

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ABSTRACT

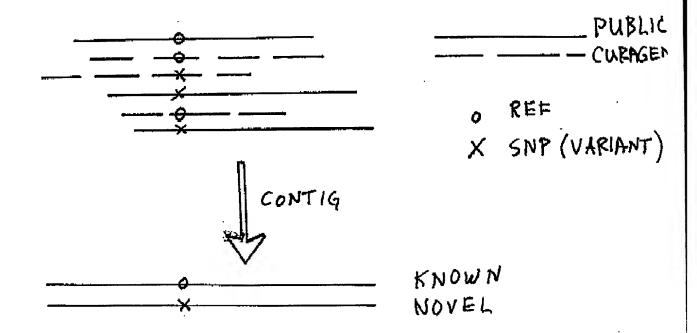
The invention provides nucleic acids containing single-nucleotide polymorphisms identified for transcribed human sequences, as well as methods of using the nucleic acids.

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Date of Deposit: December 27, 1999

Attorney Docket No. 15966-534C CIP1 (CURA-34C CIP1)

COMBINED DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and joint inventor which is claimed and for which a utility patent is sought on the invention entitled:

NUCLEIC ACIDS CONTAINING SINGLE NUCLEOTIDE POLYMORPHISMS AND METHODS OF USE THEREOF

the specification of	which:			•
was filed on U.S.S.N.	, as United St	ates non-provisional ap	oplication ·	
is attached h	ereto.			
=	have reviewed and understand the ling the claims, as amended by a			
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§365(b) of a PCT Interna States listed inventor's c	m foreign priority benefits under ny foreign application(s) for pate tional application designating at below and have also identified be ertificate or PCT International ap on on which priority is claimed.	ent or inventor's certific least one country other below any foreign appli-	cate, or §365 than the Uncation for pa	o(a) of any nited natent or
Appln.	Country	Filing Date	Priority	Claimed
Number	(if PCT, so indicate)	(dd/mm/yy)	Yes	No

I hereby claim the benefit under Title 35, United States Code, § 119(e) or §120 of any United States application(s), or §365(c) of any PCT International application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

Application No. (U.S.S.N.)	Filing Date (dd/mm/yy)	Status (Patented, Pending, Abandoned)
60/109,024	November 17, 1998	Abandoned
Not Yet Assigned	November 16, 1999	Pending
09/442,129	November 16, 1999	Pending
09/442,849	November 17, 1999	Pending

PCT International Applications designative the United States:

PCT Appln No.	US Serial No.	PCT Filing Date	Status

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

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Brett N. Dorny	35,860	John T. Prince	43,091
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John A. Harre	37,345	Carol H. Peters	45,010
Shane Hunter	41,858	Garfield B. Simms	45,109
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Robert Klauszinski	42,742	Howard Susser	33,556
Kristin E. Konzak	44,848	Shelby J. Walker	45,192
Cynthia Kozakiewicz	42,764	Martin M. Zoltick	35,745
William Marino	44,219		

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> Ivor R. Elrifi, Ph.D. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. One Financial Center Boston, Massachusetts 02111

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or patent issued thereon.

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Inventor's Cianature	Doto

Inventor's Signature

Date

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TRADOCS:1270716.1(R8H_01!.DOC)

Attorney Docket No. 15966-534C CIP1

Date of Deposit: December 27, 1999

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:

Shimkets and Leach

ASSIGNEE:

CuraGen Corporation

SERIAL NUMBER:

Not Yet Assigned

EXAMINER:

Not Yet Assigned

FILING DATE:

December 27, 1999

ART UNIT:

Not Yet Assigned

FOR:

NUCLEIC ACIDS CONTAINING SINGLE NUCLEOTIDE

POLYMORPHISMS AND METHODS OF USE THEREOF

BOX PATENT APPLICATION

Commissioner for Patents and Trademarks

Washington, D.C. 20231

STATEMENT IN SUPPORT OF COMPUTER READABLE FORM SUBMISSION UNDER 37 C.F.R. § 1.821(f)

Sir:

I hereby state that the content of the paper and computer readable forms of the Sequence Listing, submitted in the above-identified application in accordance with 37 C.F.R. § 1.821(c) and 1.821(e), respectively, are the same. No new matter is added.

Respectfully submitted,

Ivor R. Elriff, Reg. No. 39,529

Shelby J. Walker, Reg. No. 45,192

Attorney(s) for Applicants MINTZ, LEVIN, COHN, FERRIS,

GLOVSKY and POPEO, P.C.

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Boston, Massachusetts 02111

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TRADOCS:1275589.1(RC9101!.DOC)

BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE UNITED STATE PATENT AND TRADEMARK OFFICE

LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)

Michel Morency is hereby given limited recognition under 37 CFR § 10.9(b) as an employee of Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C. to prepare and prosecute patent applications wherein (1) Michel Morency represents only clients of the Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C. law firm, and (2) wherein a member of the Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C. law firm who, in turn, is a registered patent attorney or agent, is the attorney or agent of record in the applications. This limited recognition shall expire on the date appearing below, or of record in the applications. This limited recognition shall expire on the date appearing below; (i) Michel when whichever of the following events first occurs prior to the date appearing below: (i) Michel Morency ceases to lawfully reside in the United States, (ii) Michel Morency's employment with Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C. ceases or is terminated, or (iii) Michel Morency ceases to remain or reside in the United States on H-1B visa.

This document constitutes proof of such recognition. The original of this document is on file in the Office of Enrollment and Discipline of the U.S. Patent and Trademark Office.

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Expires: January 1, 2000

Karen L. Boyard, Director

Office of Enrollment and Discipline

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	25	26	27	

1.90E-178		
Himan Gene SWISSNEW-	ID:Q15166 SERUM PARAOXONASE/ARYLESTERASE 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) (SERUM ARYLDIAKYLPHOSPHATASE 3) (A-ESTERASE 3) (AROMATIC ESTERASE 3) - HOMO SAPIENS (HUMAN), 341 aa (fragment). Ipcis:SWISSPROT-ID:Q15166 SERUM PARAOXONASE/ARYLESTERASE 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) (SERUM ARYLDIAKYLPHOSPHATASE 3) (A-ESTERASE 3) - HOMO SAPIENS ESTERASE 3) - HOMO SAPIENS (HUMAN), 341 aa (fragment).	
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the true to the true that the true the true the true the true true true true true true true tru	CODING	
41 JULY - 101111	ฏ	
had had had than H	Old Old	-
Contractions and	U	
	cg43957743 1146 CAAGTTCCTCAAT CAAGTGGCAGTT[CATJTCAGGTTCTA CTGGCTCCACTTC TC CTGGCTCACTTC TC CTGGCTCCACTTC TC CTGGCTCACTTC TC	
	1146	
	cg43957743	
	58	

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24		5 (5q34)	5 (5q34)	
-		1.90E-256 5 (5q34)	1.30E-248 5 (5q34)	
1 V V (mile 1 = = = = = = = = = = = = = = = = = =	Human Gene Similar to SWISSNEW- 3.30E-00. ID:Q23917 3',5'-CYCLIG- NUCLEOTIDE PHOSPHODIESTERASE REGA (EC 3.1.4.17) (PDEASE REGA) - DICTYOSTELIUM DISCOIDEUM (SLIME MOLD), 793 aa. pcls:SWISSPROT-ID:Q23917 3',5'-CYCLIG-NUCLEOTIDE PHOSPHODIESTERASE REGA (EC 3.14.17) (PDEASE REGA) - DICTYOSTELIUM DISCOIDEUM (SLIME MOLD), 793 aa.	Human Gene SWISSPROT- ID:P47870 GAMMA- AMINOBUTYRIC-ACID RECEPTOR BETA-2 SUBUNIT PRECURSOR (GABA(A) RECEPTOR) - HOMO	Human Gene SWISSPROT- ID:P14867 GAMMA- AMINOBUTYRIC-ACID RECEPTOR ALPHA-1 SUBUNIT PRECURSOR (GABA(A) RECEPTOR) - HOMO SAPIENS (HUMAN), 456 aa.	
AT THE	esterase	gaba	gaba	
And the time that the time the time that the time that the	SILENT- CODING	SILENT- CODING	SILENT- CODING	
	Cys	ΤΫ́	Gly	_
	Cys	Tyr	Gly	_
	-	<u> </u>	-	_
	TCACCCTCAGGA CGGTGCTGTTCTGCACGACCACTACAGAAACAACCACCGAAACCAACC	TCTTCAACATCGT CCTATTGCATTAICATTATGCAACATGACCTCCAAAACATGGCCTCC	C GGATTTTGGACAG C ACTCCTAGATGG[C/TJTATGACAATC GCCTGAGACCAG	
		1631	370	
	cg43319420 963	cg3001932	cg43975899	
	25	30	31	

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CC	5243299024	1643		9	9	Gln	Glu	SILENT-	lucoamylas		7.40E-199 17 (17	17 (17q25.2
7			CCCTGGACGTCC				<u></u>		<u> </u>	GLUCOAMYLASE (EC 3.2.1.20) - HOMO SAPIENS (HUMAN), 1857	<u> </u>	
. <u>.</u> .			CCTGGACTACATG									
			GACT		+			CII ENT	ulicoamylas	EW-	7.40E-199	17
33	cg43299024	2021	TGAACGAGCCTTC G	∢	∢	Arg	δ. D.		0	ID:G2826521 MALTASE- GLUCOAMYLASE (EC 3.2.1.20) -		(1/qz3.z
			G/A]GGCTCTGAG	-						HOMO SAPIENS (HUMAN), 1857		
			GACGGCTGCCCC									
			AACA					CII ENT.	alucuronida	Human Gene SWISSPROT-		72274 44
34	cg43969076	443	AATTCCAAATGAG G	<u>√</u>		 	<u>, </u>			ID:P08236 BETA-GLUCURONIDASE PRECLIRSOR (EC 3.2.1.31) (BETA-		(/qz .
			G/AJTATTTCTGC			<u> </u>				G1) - HOMO SAPIENS (HUMAN),		
			GTTTTGATCCAG							651 aa.		1
			AC					CII ENT.	alucuronida		7.40E-80	Ç
35	cg43969014	325	-5	و ق		<u></u>	<u> </u>	CODING	se	SWISSPROT-ID:P08236 BETA- GLUCURONIDASE PRECURSOR		
			G/AJTATTTTCTGC			<u> </u>				(EC 3.2.1.31) (BETA-G1) - HOMO		
			G									15
			AC	\d \c'	A	Ala	Ala	SILENT-	glycoprotein	glycoprotein Human Gene SWISSPROI-	-	(15q15)
36	cg43065549	088	GGACCATCTCTGC			-		CODING		MEMBRANE PROTEIN BAND 4.2		
			G/AJGACGCTGTCA							(P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.		
_			၁၅				_					
		_		-		1						

The first control of the first first control of the first control of the first first control of

15	(15q15)			3.10E-249 X (Xq28)
c	>	0	0	
FOODOO	glycoprotein Human Gene SWISSPROT- ID:P16452 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.	glycoprotein Human Gene SWISSPROT- ID:Q12889 OVIDUCT-SPECIFIC GLYCOPROTEIN PRECURSOR (OVIDUCTAL GLYCOPROTEIN) (OVIDUCTIN) (ESTROGEN-	BEPENDENT OVIDOS 17 10 12 13 14 14 14 14 14 14 14 14 14 14 14 14 14	DEPENDENT OVIDUCT PROTEIN) - HOMO SAPIENS (HUMAN), 678 aa. glycoprotein Human Gene SWISSPROT- ID:Q00013 55 KD ERYTHROCYTE MEMBRANE PROTEIN (P55) - HOMO SAPIENS (HUMAN), 466 aa.
	glycoprotein	glycoprotein	glycoprotein	glycoproteir
	SILENT- CODING	SILENT. CODING	SILENT- CODING	SILENT- CODING
	Val	Val	Lys	Thr
	\ \	Val	Lys	Thr
	9	<u> </u>	<u> </u>	U
	 -	0	U	4 (5)
	ACCCCTGGAATAG AGAGGATGCTGT[1/GJTTCCTGAAGA	GCCAAATGCTC	TC GAAGGGATATAAC TGAAGCAATAAAI C/TJTTTCACGGT	CA AGGACTGTTTTC A ATTCAGCTTCAGIA CIGTGATTCCCAT GGGCTCTTCTGTG
		1141	1846	1677
	cg43065549 991	cg44004239 1	cg44004239	cg43957605
	37 0	38	38	40

Company of the second control of the second

2.00E-183 |1 (1q21)

(1q21)	1 (1921)	
2.00E-183 1 (1q21)	6.70E-183 1 (1q21)	
glycoprotein Human Gene SWISSNEW- GLYCOPROTEIN CD1A GLYCOPROTEIN CD1A GLYCOPROTEIN CD1A CELL SURFACE ANTIGEN) (T- CELL SURFACE ANTIGEN T6/LEU- 6) (HTA1 THYMOCYTE ANTIGEN) - 6) (HTA1 THYMOCYTE ANTIGEN) - 100 SAPIENS (HUMAN), 327 HOMO SAPIENS (HUMAN), 327 HOMO SAPIENS (CD1A CELL SURFACE GLYCOPROTEIN CELL SURFACE ANTIGEN) - HOMO THYMOCYTE ANTIGEN) - HOMO SAPIENS (HUMAN), 327 aa.	glycoprotein Human Gene SWISSNEW- ID:P29016 T-CELL SURFACE ID:P29016 T-CELL SURFACE GLYCOPROTEIN CD18 GLYCOPROTEIN CD18 ANTIGEN) - Aa. pcls:SWISSPROT-ID:P29016 T- CELL SURFACE GLYCOPROTEIN CELL SURFACE GLYCOPROTEIN CD18 PRECURSOR (CD18 ANTIGEN) - HOMO SAPIENS (HUMAN), 333 aa.	
ycoprotein	glycoprotein	
Pro SILENT- 9 CODING	SILENT- CODING	
Pro	Гел	
Pro Diagram	nen 	-
ATGTCTCAGGATT C CTACCCAAAGCCI C/TJGTGTGGGTGA TGTGGATGCGGG GTG	TGGCAATAATAGT C GCCTTCCTTGCTI C/TJCTTTTGCTAT GCCTTGCATTATG GT	
1229	1210	
cg40915005	cg40356255	
14	42	

	1 (1921)	14 (14q11.2)
7.60E-127	1.60E-119 1 (1q21)	9.90E-70)
glycoprotein Human Gene Homologous to SWISSNEW-ID:P01732 T-CELL SURFACE GLYCOPROTEIN CD8 ALPHA CHAIN PRECURSOR (T-LYMPHOCYTE DIFFERENTIATION ANTIGEN T8/LEU-2) - HOMO SAPIENS (HUMAN), 235 aa. pcls:SWISSPROT-ID:P01732 T-CELL SURFACE GLYCOPROTEIN CD8 ALPHA CHAIN PRECURSOR (T-LYMPHOCYTE DIFFERENTIATION ANTIGEN T8/LEU-2) - HOMO SAPIENS (HUMAN), 235 aa.	glycoprotein Human Gene Homologous to SWISSPROT-ID:P02743 SERUM AMYLOID P-COMPONENT PRECURSOR (SAP) (9.5S ALPHA- 1-GLYCOPROTEIN) - HOMO SAPIENS (HUMAN), 223 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P16452 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.
glycoprotein	glycoprotein	glycoprotein
SILENT- CODING	SILENT- CODING	SILENT- CODING
ne	 	Gly
ne Ten	Val	Gly
—	⋖	⋖
O	o	O
CTGTGATATCTAC C ATCTGGGCGCCC[C/TJTGGCCGGGA CTTGTGGGGTCCT TCT	AGGGTCTGCGAC AGGGTTACTTTGT G/AJGAAGCTCAGC CCAAGATTGTCCT GG	ATGGCCAGTGCT GGGTCTTTGCTG G[C/A]GTGACCAC CACAGTGCTGCG CTGCC
1183	544	1242
cg44004667 1183	cg43068999	cg41568631
43	44	45

14 (14q11.2)	1 (1922)	1 (1922)		
9.90E-70	3.00E-52	3.00E-52	3.60E-120	4.30E-216
glycoprotein Human Gene Similar to SWISSPROT-ID:P16452 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.	glycoprotein Human Gene Similar to SPTREMBL-ID:Q91406 IP1=CNS MYELIN P0-LIKE GLYCOPROTEIN -UNKNOWN, 202 aa.	glycoprotein Human Gene Similar to SPTREMBL-ID:Q91406 IP1=CNS MYELIN P0-LIKE GLYCOPROTEIN -UNKNOWN, 202 aa.	Human Gene Homologous to SWISSPROT-ID:Q12099 PROBABLE ATP-DEPENDENT RNA HELICASE FAL1- SACCHAROMYCES CEREVISIAE (BAKER'S YEAST), 399 aa.	Human Gene SWISSPROT- ID:P50458 HOMEOBOX PROTEIN LH-2 - HOMO SAPIENS (HUMAN), 423 aa.
glycoprotein	glycoprotein	glycoprotein	helicase	нотеорох
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Glý	Arg	Asn	Ala	Asn
Gly	Arg	Asn	Ala	Asn
ග	F	ပ	O	—
O	ပ	 -	ဖ	ပ
GCTCTGTGGAGT CCATCAAGAATGG [C/G]CTGGTCTAC ATGAAGTACGACA CGC	GCATCCAGTGGG TAGGGGACCCTC G[C/T]TGGAAGGA TGGCTCCATTGTC ATAC	TACACAACCTAGA CTACAGTGACAA[1/C]GGCACGTTCA CTTGTGACGTCAA AA	AGTCCCTTCTCCG G TGGCACCTACGC[G/CJTATGGTTTTG AGAAGCCCTCTG CCA	AGTCTTACTTTGC C CATTAACCACAA[C /TJCCCGACGCCAA GGACTTGAAGCA GGCTTGAAGCA
1545	361	409	465	1353
cg41568631	cg41603916	cg41603916	cg34317662	cg43983917
46	47	48	64	50

	2			2 (2q21)
4.30E-216	2.60E-188	1.10E-123	1.30E-113	0
Human Gene SWISSPROT- ID:P50458 HOMEOBOX PROTEIN LH-2 - HOMO SAPIENS (HUMAN), 423 aa.	Human Gene SWISSPROT- ID:P28356 HOMEOBOX PROTEIN HOX-D9 (HOX-4C) (HOX-5.2) - HOMO SAPIENS (HUMAN), 342 aa.	Human Gene Homologous to SWISSPROT-ID:P17509 HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (HU-2) - HOMO SAPIENS (HUMAN), 224 aa.	Human Gene Homologous to SWISSPROT-ID:P09629 HOMEOBOX PROTEIN HOX-B7 (HOX-2C) (HHO.C1) - HOMO SAPIENS (HUMAN), 217 aa.	Human Gene SWISSPROT- ID:P09848 LACTASE-PHLORIZIN HYDROLASE PRECURSOR (EC 3.2.1.108) (EC 3.2.1.62) (LACTASE- GLYCOSYLCERAMIDASE) - HOMO SAPIENS (HUMAN), 1927 aa.
homeobox	homeobox	homeobox	homeobox	hydrolase
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Asp	Ala	Lys	Lys	Arg
Asp	Ala	Lys	Lys	Arg
-	H	«	U	O
U	ပ	ဖ	⊢	A
ACTITGCCATTAA CCACACCCGAI C/TJGCCAAGGACT TGAAGCAGCTCG CGC	TGGAGCGAGCGT GGATCCAGTTCG C[G/T]GCGGGGTT GTTTGGGTCAAGT	GTTACCAGACGCT GGAGCTGGAGAA[G/A]GAGTTTCACT ACAATCGCTACCT GA	TCAGGTAGCGATT GTAGTGAAATTCIT /CJTTCTCCAGCTC CAGGGTCTGGTA GC	GGGAAGCATTTG CCAATCAGTCCAG [A/G]GCGGAAAGG GATGCCTTCCTGC AGG
1359	979	689	810	1124
cg43983917 1359	cg42730678	cg42714160	cg43959084	cg42359655
51	-52	53	54	55

2 (2q21)	2 (2q21)	16 (16q22)	15
0	0	2.00E-220	0
Human Gene SWISSPROT- ID:P09848 LACTASE-PHLORIZIN HYDROLASE PRECURSOR (EC 3.2.1.108) (EC 3.2.1.62) (LACTASE- GLYCOSYLCERAMIDASE) - HOMO SAPIENS (HUMAN), 1927 aa.	Human Gene SWISSPROT- ID:P09848 LACTASE-PHLORIZIN HYDROLASE PRECURSOR (EC 3.2.1.108) (EC 3.2.1.62) (LACTASE- GLYCOSYLCERAMIDASE) - HOMO SAPIENS (HUMAN), 1927 aa.	hydroxyster Human Gene SPTREMBL- oid HYDROXYSTEROID DEHYDROGENASE TYPE 2 - HOMO SAPIENS (HUMAN), 405 aa.	Human Gene TREMBLNEW- ID:G2114410 INTERLEUKIN-16 - HOMO SAPIENS (HUMAN), 631 aa.
hydrolase	hydrolase	hydroxyster oid	interleukin
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
H S	Gly	Val	Pro
His S	Gly	Val	Pro
—	H	A	—
O	O	O	O
ACAGCCAGCGGT C TTGGCCTGCACCA [C/I]GTCAACTTCA GCGACAGCAGCA AGT	ATCTGGTCACCCT C GCAGAACCTGGG[C/IJGTGTCCCACT ACCGTTTTCCAT CT	TGGTGTGGGCCT C TGGTGAACTCTAG [C/A]ACGCGGCTA ATGTCTCCTGGTT TGG	GGAAGCTGACTC CAGAGGCCATGC CIC/TIGACCTCAA CTCCTCCACTGAC
	4340	1329	1689
cg42359655 2468	cg42359655 4340	cg43998672	cg43922672
56	57	28	59

7 (7p21)	5 (5p13)
3.40E-108 7 (7p21)	3.10E-249 5 (5p13)
Human Gene Homologous to SWISSPROT-ID:P05231 INTERLEUKIN-6 PRECURSOR (IL- 6) (B-CELL STIMULATORY FACTOR 2) (BSF-2) (INTERFERON BETA-2) (HYBRIDOMA GROWTH FACTOR) - HOMO SAPIENS (HUMAN), 212 aa.	interleukinre Human Gene SWISSNEW- cept ID:P16871 INTERLEUKIN-7 RECEPTOR ALPHA CHAIN PRECURSOR (IL-7R-ALPHA) (CDW127) (CD127 ANTIGEN) - HOMO SAPIENS (HUMAN), 459 aa. pcls:SWISSPROT-ID:P16871 INTERLEUKIN-7 RECEPTOR ALPHA CHAIN PRECURSOR (IL-7R-ALPHA) (CDW127) (CD127 ANTIGEN) - HOMO SAPIENS (HUMAN), 459 aa.
interleukin	interleukinre cept
SILENT- CODING	SILENT- CODING
\ \ 	His S
\ \	His
O	H-
ڻ ت	O
GTAGTGAGGAAC G AAGCCAGAGCTG T[G/C]CAGATGAG TACAAAAGTCCTG ATCC	AGTTGGAAGTGAA C TGGATCGCAGCA{ C/IJTCACTGACCT GTGCTTTTGAGGA CC
030	181
cg42908571 630	cg43942050
09	6

ო	ო	10
0	0	0
Human Gene SWISSNEW- ID:P42336 PHOSPHATIDYLINOSITOL 3- KINASE CATALYTIC SUBUNIT, ALPHA ISOFORM (EC 2.7.1.137) (PI3-KINASE P110 SUBUNIT ALPHA) (PTDINS-3-KINASE P110) (PI3K) - HOMO SAPIENS (HUMAN), 1068 aa. [pcis:SWISSPROT- ID:P4236 PHOSPHATIDYLINOSITOL 3- KINASE CATALYTIC SUBUNIT, ALPHA ISOFORM (EC 2.7.1.137) (PI3-KINASE P110 SUBUNIT ALPHA) (PTDINS-3-KINASE P110) (PI3K) - HOMO SAPIENS (HUMAN), 1068 aa.	Human Gene SPTREMBL- ID:Q63553 SNF1-RELATED KINASE - RATTUS NORVEGICUS (RAT), 746 aa.	Human Gene SWISSPROT- ID:Q04759 PROTEIN KINASE C, THETA TYPE (EC 2.7.1) (NPKC- THETA) - HOMO SAPIENS (HUMAN), 706 aa.
kinase	kinase	kinase
SILENT-	SILENT- CODING	SILENT- CODING
<u>•</u>	Asp	Phe
<u>=</u>	Asp	Phe
 -	H	—
O	O	O
TAAATATTCGAGA (CATTGACAGAT[CATTGACAAGAT[CAGGTATCTACCAAGATGTGAAGATGTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACCAAGGTATCTACAGGTATCTACAGGTATCTACAGGTATCTACAGGTATCTACAGGTATCTACAGGTATCAGGTATCTACAGGTATCTACAGGTATCTACAGGTATCTACAGGTATCAGGTAGAGTAGAGTAGAGTAGAGTAGAGTAGAGTAGAGAGTAGAGTAG	AGATCTTTGAGGA AGGGGAATCTGA[C/TJGATGAGTTTG ACATGGATGAGAA TC	TTCTGACGCACAT GTTTGTACATT[C /TJCAGACCAAGGA AAACCTCTTTTT G
1249	1693	1438
cg43145505 1249	cg43918241	cg43090990
62	63	64

21 (21q22.1)	X (Xq21.3)	1 (1q21 <u>)</u>
0	0	9.80E-308 1 (1q21)
Human Gene SWISSPROT- ID:Q13627 SERINE/THREONINE- SPECIFIC PROTEIN KINASE MINIBRAIN HOMOLOG (EC 2.7.1) (HP86) (DYRK) - HOMO SAPIENS (HUMAN), 763 aa.	Human Gene SWISSPROT- ID:Q06187 TYROSINE-PROTEIN KINASE BTK (EC 2.7.1.12) (BRUTON'S TYROSINE KINASE) (AGAMMAGLOBULINAEMIA TYROSINE KINASE) (ATK) (B CELL PROGENITOR KINASE) (BPK) - HOMO SAPIENS (HUMAN), 659 aa.	Human Gene SPTREMBL- ID:Q16715 PYRUVATE KINASE (EC 2.7.1.40) - HOMO SAPIENS (HUMAN), 587 aa (fragment).
kinase	kinase	kinase
SILENT- CODING	SILENT- CODING	SILENT- CODING
Lys	Cys	Arg
Lys	Cys	Arg
O	U	O
∢	⊢	K
TTAGTATCATTCA A CTGTGATCTAAA[A /G]CCTGAAAATAT CCTTCTTGTAAC C	AGGTATATACCAT CATGTACAGTTG[T /C]TGGCATGAGAA AGCAGATGAGCG TC	TGGCTCCGGCTA CACCAACATCATG [ACJGGGTGCTAA GCATATCCTGAGA CGC
2339	2062	1744
cg43969763 2339	cg42879455 2062	cg42659872
65	99	29

7 (7q21.3)	41	11 (20p13)
1.60E-220 7 (7	3.80E-219	2.00E-215
Human Gene SWISSPROT- ID:Q16654 [PYRUVATE DEHYDROGENASE(LIPOAMIDE)] KINASE ISOZYME 4 PRECURSOR (EC 2.7.1.99) (PYRUVATE DEHYDROGENASE KINASE ISOFORM 4) - HOMO SAPIENS (HUMAN), 411 aa. [pds:SPTREMBL-ID:Q16654 PYRUVATE DEHYDROGENASE KINASE ISOFORM 4 - HOMO SAPIENS (HUMAN), 411 aa.	Human Gene SWISSPROT- ID:Q15119 [PYRUVATE DEHYDROGENASE(LIPOAMIDE)] KINASE ISOZYME 2 PRECURSOR (EC 2.7.1.99) (PYRUVATE DEHYDROGENASE KINASE ISOFORM 2) - HOMO SAPIENS (HUMAN), 407 aa. pcls:SPTREMBL- ID:Q15119 PYRUVATE DEHYDROGENASE KINASE - HOMO SAPIENS (HUMAN), 407 aa.	Human Gene SWISSPROT- ID:P19138 CASEIN KINASE II, ALPHA CHAIN (CK II) (EC 2.7.1.37) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 391 aa.
kinase	kinase	kinase
SILENT- CODING	SILENT- CODING	SILENT- CODING
Ala	Arg	Thr
Ala	Arg	Thr
U		
A	O	ပ
GCTTGCCAATTTC A TCGTCTGTATGC[ACJAAGTACTTTC AAGGAGATCTGAA TC	CTGTGGAGTACAT GTAGCTGAAGAGI C/TJCGCTCAATCT TCCTCAAGGGAAC AC	ACATCATATTGGC GCTGCTGACGGGI C/TJGTACTGCCCC CTGGCATGCTAGA TG
1323	526	1448
cg42506800 1323	cg43966621	cg43917871
89 9	69	70

11 (20p13)	16	11	2
2.00E-215	7.80E-173	2.10E-154	7.90E-283
Human Gene SWISSPROT- ID:P19138 CASEIN KINASE II, ALPHA CHAIN (CK II) (EC 2.7.1.37) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 391 aa.	Human Gene SPTREMBL- ID:Q15599 TYROSINE KINASE ACTIVATOR PROTEIN 1 (TKA-1) - HOMO SAPIENS (HUMAN), 450 aa.	Human Gene SPTREMBL- ID:Q27467 SIMILARITY TO TYROSINE-PROTEIN KINASE - CAENORHABDITIS ELEGANS, 1280 aa.	Human Gene SWISSPROT- ID:Q04771 ACTIVIN RECEPTOR TYPE I PRECURSOR (EC 2.7.1) (ACTR-I) (SERINE/THREONINE- PROTEIN KINASE RECEPTOR R1) (SKR1) (ACTIVIN RECEPTOR-LIKE KINASE 2) (ALK-2) (TGF-B SUPERFAMILY RECEPTOR TYPE I) (TSR-I) - HOMO SAPIENS (HUMAN), 509 aa.
kinase	kinase	kinase	kinaserecep tor
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Ala	Ser	Asn	Ala
Ala	N Pi	Asn	Ala
O	A	ပ	U
—	ပ	 -	—
CAGTGTAGAAATA GGGGTGCTCCATI T/GJGCCTCTCTTG CAGTAAGCCGTG ACT	AGCTCAATGGTG GCTCTGCGTGCT C[G/A]TCCCGAAG TGACCTGCCTGGT TCCG	AATTCAACCCACT CATCTATGGCAA[T /CJGATGTGGATTC TGTGGATGTTGCA	AGACCCCGCCGT CCCCTGGCCAAG C[T/C]GTGGAGTG CTGCCAAGGGGA CTGGT
1526	912	1765	610
cg43917871 1526	cg44131752	cg43969473 1765	cg44025829
71	72	73	74

9	6 (6p21.3)	6 (6p21.3)	6 (6p21.3)	6 (6p21.3)
1.20E-247 6	9.10E-147	3.70E-134	3.70E-134	3.70E-134
Human Gene SPTREMBL- ID:Q02646 MHC BINDING PROTEIN 2 - HOMO SAPIENS (HUMAN), 2500 aa.	Human Gene Homologous to SWISSPROT-ID:P28068 CLASS II HISTOCOMPATIBILITY ANTIGEN, M BETA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 263 aa.	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.
МНС	MHC	МНС	МНС	MHC
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Pro	ne T	Pen	ren	Leu
Pro	ne ₁		nen	ren
٧	d	ව	⋖	∢
ඉ	ග	∢	O	O
CTCACGCTTTGCA GTCATCTGGTCC[GAJCCTAGCACTC CCTCCTCCTCG GC	TTAACACGAGGGA GCCTGTGATGCTI G/AJGCCTGCTATG TGTGGGGCTTCTA TC	CCCCTGTGATCAA A TATCACCTGGCT[A/G]CGCAACGGC CAAACTGTCACTG AGG	CACCACCAGATG CCATGGAGACCC T[G/A]GTCTGTGC CCTGGGCCTGGC CATCG	CCATGGAGACCC TGGTCTGTGCCCT [G/A]GGCCTGGCC ATCGGCCTGGTG GGCT
1107	632	644	857	869
cg43318277	cg43966144	cg42686658	cg42686658	cg42686658
75	76	77	82	62

cg42686658 881		TGGTCTGTGCCCT (GGGCCTGCAT) C/TJGGCCTGGTGGGCGTGGTGGGGCTGGTGGGGGGGGGG	U		<u>a</u>	<u>e</u>	SILENT-	MHC	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.	3.70E-134 6 (6	6 (6p21.3)
893 TGGGC TCGGC G[C/G]T GGCCA CATCA	TGGGC TCGGC G[C/G]T GGGCA CATCA	TGGGCCTGGCCA (TCGGCCTGGTGGGGCCTGGTGGTGGTGGTGGTGGTGGTGG	O	0	Gly	Gly	SILENT- CODING	W HC	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.	3.70E-134	6 (6p21.3)
905 TCGGC GCTTC G[C/T]A CATCA ACAT	TCGGC GCTTC G[C/T]A CATCA ACAT	TCGGCCTGGTGG GCTTCCTCGTGG G[C/T]ACCGTCCT CATCATCATGGGC ACAT	U	_	Gly	Gly	SILENT- CODING	MHC	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.	3.70E-134	6 (6p21.3)
279 GTTTC CCCTG ATJGCA GGACC GTC	GTTTC CCCTG A/TJGC/ GGACC 3TC	GTTTCCTCATTAG / CCCTGTGACCCCI A/TJGCACACGCAG GGACCTACAGAT GTC	∀	<u> </u>	Pro	Pro	SILENT- CODING	MHC	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	1.80E-113	<u>උ</u>
492 TTGACA TCTATC GAJGG CATGAA TCC	TTGAC/ TCTATC G/AJGG/ CATGA/ TCC	TTGACATCTACCA CTCTATCAGGA GAIGGGGAAGCC CATGAACTTAGGC	9	A A	Glu	Olu	SILENT- CODING	MHC	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	1.80E-113	1 0

19	19	19	20	3 (3p24)
1.80E-113 19	1.80E-113	1.80E-113	0	0
Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene SPTREMBL- ID:Q14193 H-DRK1 K(+) CHANNEL - HOMO SAPIENS (HUMAN), 858 aa.	misc_chann Human Gene SPTREMBL- ID:Q14524 SODIUM CHANNEL ALPHA SUBUNIT - HOMO SAPIENS (HUMAN), 2016 aa.
MHC	МНС	MHC	misc_chann el	misc_chann el
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Th	Phe		Th.	Cys
Thr	Phe	ren [Thr	Cys
4	—	U	 	H-
H	ပ	⊢	ပ	O
CTTCTAGTAGTTG GCCTTCACCCAC T/AJGAACCAAGCT TCAAAACTGGTAT CG	GGTACTCAGTGG CCATCATCCTTI C/TACCATCCTTC CCTTCTTTCTCCT TC	TGGCCATCATCCT CTTCACCATCCTT /cjccCTTCTTTCT cCTTCATCGCTGG	AGGAGCTCAAGC GTGAGGCCGAGA C[C/T]CTACGGGA GCGGGAAGGCGA GGAGT	TCATGGGCAACCT C AAGGCACAAGTG C/TJGTGCGCAACT TCACAGCGCTCAA CG
669	774	783	649	066
cg38337333 699	cg38337333	cg38337333	cg43984759	cg39660131
85	98	87	88	68

19 (19q13.1)			8 (8p11.2)
2.20E-113 19 (19 (19)	7.90E-79	7.90E-79	6.10E-70
misc_chann Human Gene Homologous to SWISSPROT-ID:Q07699 SODIUM CHANNEL BETA-1 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 218 aa. pcls:TREMBLNEW-ID:G2804300 VOLTAGE-GATED SODIUM CHANNEL BETA-1 SUBUNIT - HOMO SAPIENS (HUMAN), 218 aa.	misc_chann Human Gene Similar to SPTREMBL- 7.90E-79 el ID:P91197 SIMILAR TO LIGAND- GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.	misc_chann Human Gene Similar to SPTREMBL- 7.90E-79 el ID:P91197 SIMILAR TO LIGAND- GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.	misc_chann Human Gene Similar to SPTREMBL- 6.10E-70 ID:P91197 SIMILAR TO LIGAND- GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.
misc_chann el	misc_chann el	misc_chann el	misc_chann el
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
n O	Asp	Cys	P 0
nje	Asp	Cys	Pro
O	F	—	O
∢	O	O	4
CGGAATACCTGG CCATCACCTCTGA [WG]AGCAAAGAG AACTGCACGGGC GTCC	AGAGTGGCGAGT (GGGTCATCGTGGAGTCATCGTGGCGTGGGGCGTGGGGGGGG	ACAACACCAGGAA C GTACGAGTGCTG C/TJGCCGAGATCT ACCCGGACATCA CCT	AGAGGCTCTTTCT A GCAGAAACTTCC[A/CJAAATTACTTT GCATGAAAGATCA TG
717	870	606	1160
cg44963814 717	cg21413267	cg21413267	cg3000465
06	91	92	63

11 (11q22)	11 (11q22)		14 (14q24)
0	0	1.10E-115	0
Human Gene SWISSNEW- ID:P06401 PROGESTERONE RECEPTOR (PR) - HOMO SAPIENS (HUMAN), 933 aa.lpcls:SWISSPROT-ID:P06401 PROGESTERONE RECEPTOR (PR) - HOMO SAPIENS (HUMAN), 933 aa.	Human Gene SWISSNEW- ID:P06401 PROGESTERONE RECEPTOR (PR) - HOMO SAPIENS (HUMAN), 933 aa. pcls:SWISSPROT-ID:P06401 PROGESTERONE RECEPTOR (PR) - HOMO SAPIENS (HUMAN), 933 aa.	Human Gene Homologous to SWISSPROT-ID:P07992 DNA EXCISION REPAIR PROTEIN ERCC-1 - HOMO SAPIENS (HUMAN), 297 aa.	Human Gene SPTREMBL- ID:Q99907 LATENT TRANSFORMING GROWTH FACTOR-BETA-BINDING PROTEIN- 2 - HOMO SAPIENS (HUMAN), 1821 aa.
nucl_recpt	nucl_recpt	nuclease	oncogene
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
His	Gln	Asn	Thr
His Sign	Gin	Asn	Thr
H	<u>ن</u>	0	<u>ග</u>
ပ	V	A	∢
GTCTAGGATGGA GATCCTACAAACA [C/I]GTCAGTGGG CAGATGCTGTATT TTG	ATAACTTGCATGA TCTTGTCAAACAĮA /GJCTTCATCTGTA CTGCTTGAATACA T	TTACGTCGCCAAA A TTCCCAGGGCAC[A/GJTTGCGCACGA ACTTCAGTACGGGACACAATTCAGTACGGGATATTCAGTACGGGATATTCAGTACGGGAATTACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACGGGAATACAGTACAGAATACAGGAATACAGTACAAAAATACAAAAAAAA	TCCCTGTGACCCA A GGCAGGTGCATG[A/G]GTGACACTGG TCGTGACCTGGC CAG
	4114	713	4226
cg30421838 3766	cg30421838	cg43947341	cg43939230
6	ى 2	96	26

10	22 (22q11)	1 (1q25)	
α	2.40E-84		2.40E-155
Human Gene SWISSPROT- ID:P31314 HOMEOBOX PROTEIN HOX-11 (TCL-3 PROTO- ONCOGENE) - HOMO SAPIENS (HUMAN), 330 aa.	Human Gene Similar to SWISSPROT-ID:Q64010 PROTO- ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK) - MUS MUSCULUS (MOUSE), 304 aa.	Human Gene SWISSPROT- ID:P19878 NEUTROPHIL CYTOSOL FACTOR 2 (NCF-2) (NEUTROPHIL NADPH OXIDASE FACTOR 2) (P67- PHOX) - HOMO SAPIENS (HUMAN), 526 aa.	phosphoryla Human Gene SWISSPROT- se ID:P00491 PURINE NUCLEOSIDE PHOSPHORYLASE (EC 2.4.2.1) (INOSINE PHOSPHORYLASE) (PNP) - HOMO SAPIENS (HUMAN), 289 aa.
oncogene	oncogene	oxidase	phosphoryla se
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Ala	<u>e</u>	Leu	Pro
Ala	<u>=</u>	leu.	Pro
	L	-	⋖
ပ	O	O	O
CGGCACAGGC C CGCTCGCCGGAG C[C/T]GTGGCCCA CCCCAGCCCCT	AGAACTCGCGGG TCTCCCACTACAT C/TJATCAACTCGC TGCCCAACCGC GTT	CTGCAACTACCTT GAACCAGTTGAG[C/TJTGCGGATCCA CCCTCAGCAGCA GCC	CAGCATGACCTG GCACTGTACTTCG [G/A]GGAAAGTTG GGGATTTCACCGT AGT
1447	742	963	1310
cg42674136 1447	cg41972699	cg42849556	cg43996195
86	66	100	101

22	ю О
2.40E-155	5.40E-62
phosphoryla Human Gene SWISSPROT- se ID:P00491 PURINE NUCLEOSIDE PHOSPHORYLASE (EC 2.4.2.1) (INOSINE PHOSPHORYLASE) (PNP) - HOMO SAPIENS (HUMAN), 289 aa.	Human Gene Similar to SWISSNEW- 6.40E-62 ID:P53999 ACTIVATED RNA POLYMERASE II TRANSCRIPTIONAL COACTIVATOR P15 (PC4) (P14) - HOMO SAPIENS (HUMAN), 126 aa. pcls:SWISSPROT-ID:P53999 ACTIVATED RNA POLYMERASE II TRANSCRIPTIONAL COACTIVATOR P15 (PC4) (P14) - HOMO SAPIENS (HUMAN), 126 aa.
phosphoryla se	polymerase
SILENT- CODING	SILENT. CODING
His S	<u>=</u>
된 SH	<u>e</u>
⋖	—
ග	⋖
TTGCAACTTGAGG G TCGGTGCTTAGT[G/A]TGAGACAGAA GCCATTCTGCAGT GT	TTTACAGTTTTCTT A ACTGCATCATC[A/ TJATGTCAGAAATC TGTTCCTTCAGCT
1421	372
cg43996195 1421	cg43948227
102	103

4.40E-241
potassium_ Human Gene SWISSNEW- channel D:P48050 INWARD RECTIFIER POTASSIUM CHANNEL 4 (POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 4) (HIPPOCAMPAL INWARD RECTIFIER) (HIR) (HRK1) (HIRK2) (KIR2.3) - HOMO SAPIENS (HUMAN), 445 aa.lpcis:SWISSPROT-ID:P48050 INWARD RECTIFIER POTASSIUM CHANNEL INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 4) (HIPPOCAMPAL INWARD RECTIFIER) (HIR) (HRK1) (HIRK2) (KIR2.3) - HOMO SAPIENS (HUMAN), 445 aa.
potassium_ channel
SILENT- CODING
Ser
Ser
ပ
4
cg43333426 1302 AGAGCCACTACCAA A GGTGGACTACTC[A/G]CGTTTTCACA AGACCTACGAGG TGG
1302
cg43333426
104

9	8	14 (14q32.1)
1.60E-227	1.20E-208 2	4.40E-83
Human Gene SWISSPROT- ID:P48051 G PROTEIN-ACTIVATED INWARD RECTIFIER POTASSIUM CHANNEL 2 (GIRK2) (POTASSIUM CHANNEL, INWARDLY RECTIFYING, SUBFAMILY J, MEMBER 6) (KATP-2) (BIR1) (KIR3.2) - HOMO SAPIENS (HUMAN), 423 aa.lpcls:TREMBLNEW-ID:G1518526 INWARDLY RECTIFYING POTASSIUM CHANNEL KIR3.2 - HOMO SAPIENS (HUMAN), 423 aa.	proteaseinhi Human Gene SWISSPROT- b ID:P07093 GLIA DERIVED NEXIN PRECURSOR (GDN) (PROTEASE NEXIN I) (PN-1) (PROTEASE INHIBITOR 7) - HOMO SAPIENS (HUMAN), 398 aa.	proteaseinhi Human Gene Similar to SWISSPROT-ID:P17475 ALPHA-1- ANTIPROTEINASE PRECURSOR (ALPHA-1-ANTITRYPSIN) (ALPHA- 1- PROTEINASE INHIBITOR) - RATTUS NORVEGICUS (RAT), 411 aa.
potassium_ channel	proteaseinhi b	proteaseinhi b
SILENT. CODING	SILENT. CODING	SILENT- CODING
Asp	 	Thr
Asp	<u>a</u>	Thr
ပ	ပ	 -
H	U	O
TCACACCTGTCCT GACCCTGGAGGA[T/C]GGGTTCTACG AAGTTGACTACAA CA	GCAGGATCACCT GCACCCTCTTGG G[C/G]ACCATGAT GCTCATCCAGCTG TCTA	AGTCAGACACCA GCTTAGAAATGAC [C/T]ATGGGCAAT GCCTTGTTTCTTG ATG
1683	1081	624
cg43051431 1683	cg43920929	cg43059041
105	106	107

3 (3p)	17	7	20 (20q12)	ω
2.90E-260 3 (3p)	1.40E-180	2.40E-114		8.30E-58
Human Gene SPTREMBL- ID:Q92777 SYNAPSIN IIB - HOMO SAPIENS (HUMAN), 478 aa.	Human Gene SPTREMBL- ID:Q28686 50-KDA DYSTROPHIN- ASSOCIATED GLYCOPROTEIN PRECURSOR - ORYCTOLAGUS CUNICULUS (RABBIT), 387 aa.	Human Gene Homologous to TREMBLNEW-ID:G1703715 PANTOPHYSIN=SYNAPTOPHYSIN HOMOLOG - MUS SP, 261 aa.	Human Gene Similar to SWISSPROT-ID:P02585 TROPONIN C, SKELETAL MUSCLE - HOMO SAPIENS (HUMAN), 159 aa.	Human Gene Similar to SWISSPROT-ID:P02535 KERATIN, TYPE I CYTOSKELETAL 10 (CYTOKERATIN 10) (56 KD CYTOKERATIN) (KERATIN, TYPE I CYTOSKELETAL 59 KD) - MUS MUSCULUS (MOUSE), 569 aa.
struct	struct	struct	struct	struct
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Leu	ng Oln	ren	Thr	Arg
ren len	Glu	nen	고 다	Arg
<u> </u>	⋖	O	⋖	<u>ق</u>
U	O	K	O	O
GGAGGACAGGCA C ACTCATCACCGAA [C/TJTAGTCATCAG CAAGATGAACCAG	ACCCGTTCTTCTG CCCACCACTGA[G/A]GCCCCAGAC CGTGACTTCTTGG TGG	TCTGGAAGCCGG ACATCCTCTGAGC [AGJAGTCGACTG ATCCGCTGGCGA	TCATCAGAGATTC GATCTCCTCGTC CAJGTCACGTGCT CCCGGAGGCCC TGA	GCTTTGAGGAGG AGGCGCGGTTGC G[C/G]GACGACAC TGAGGCGGCCAT CCGCG
1385	1002	2160	497	788
cg40148056 1385	cg42894986	cg43961212	cg42898003	cg43960684
108	109	110	111	112

ω	16
9.20E-83	7.70E-79
Human Gene Similar to SPTREMBL- 9.20E-83 ID:Q42761 SQUALENE SYNTHASE (EC 2.5.1.21) (FARNESYL- DIPHOSPHATE FARNESYLTRANSFERASE) (FARNESYLTRANSFERASE) (PRESQUALENE-DI- DIPHOSPHOSPHATE SYNTHASE) - GLYCYRRHIZA GLABRA, 412 aa.	Human Gene Similar to SWISSNEW- 7.70E-79 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.pcls:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.
synthase	synthase
SILENT	SILENT- CODING
Leu	Á Ö
ne n	oj.
U	-
ဖ	4
TTCGGAAAGGGC G AAGCAGTGACCT [G/C]ATGATGGAT GCCACCAATATGC CAG	ACACCCACAGCA A GITTTGGTTTAGG[A/I]TTATCTGTAAA TGGAAGGTTCTG GC
<u>.</u>	
cg43958714 1049	cg43124627 901
113	4

9.90E-70																
Human Gene Similar to SWISSNEW- 9.90E-70	ID:P53556 8-AMINO-7-	OXONONANOATE SYNTHASE (EC	2.3.1.47) (7-KETO-8-AMINO-	PELARGONIC ACID SYNTHETASE)	(7-KAP SYNTHETASE) (L-ALANINE-	-PIMELYL COA LIGASE) -	BACILLUS SUBTILIS, 389	aa. pcls:SWISSPROT-ID:P53556 8-	AMINO-7-OXONONANOATE	SYNTHASE (EC 2.3.1.47) (7-KETO-	8-AMINO- PELARGONIC ACID	SYNTHETASE) (7-KAP	SYNTHETASE) (L-ALANINE	PIMELYL COA LIGASE) - BACILLUS	SUBTILIS, 389 aa.	
synthase																
SILENT-	CODING															
Ala																
Ala																
L																
A																
TCTTCTCCAACAG	TCTGCCACCGC	ATIGTCGTTGGCT	GCGCCTCCAAGG	222))											
ca43968419 906)										,					
115																

7.40E-65	7.40E-65
Human Gene Similar to SWISSNEW- 7.40E-65 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa. [pcls:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.	Human Gene Similar to SWISSNEW- 7.40E-65 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa. picis:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA LIGASE) - BACILLUS SUBTILIS, 572 aa.
synthase	synthase
SILENT- CODING	SILENT- CODING
Ten	Lys
Leu	Lys
A	4
ပ	ပ
TTGTGGTCCTGGC G CTCGCAGTTCCT[G/AJTCCCATGACC CAGAACAGCTCAC CA	TCACAGGGAAAAT TCAACGAGCCAA[GA]CTTCGAGACA AGGAGTGGAAGA TGT
1484	1622
cg43064068 1484	cg43064068
116	117

11		11	4	4
1.70E-241 11	1.70E-241	1.70E-241	1.60E-236	1.60E-236
Human Gene SWISSPROT- ID:P14416 D(2) DOPAMINE RECEPTOR - HOMO SAPIENS (HUMAN), 443 aa.	Human Gene SWISSPROT- ID:P14416 D(2) DOPAMINE RECEPTOR - HOMO SAPIENS (HUMAN), 443 aa.	Human Gene SWISSPROT- ID:P14416 D(2) DOPAMINE RECEPTOR - HOMO SAPIENS (HUMAN), 443 aa.	Human Gene SWISSPROT- ID:P25101 ENDOTHELIN-1 RECEPTOR PRECURSOR (ET-A) - HOMO SAPIENS (HUMAN), 427 aa.	Human Gene SWISSPROT- ID:P25101 ENDOTHELIN-1 RECEPTOR PRECURSOR (ET-A) - HOMO SAPIENS (HUMAN), 427 aa.
tm7	tm7	tm7	tm7	tm7
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
i I	ren	Pro	i Si	n O
म ड	Leu	Pro	E S	ngo
<u> </u>	H-	∢	<u> </u>	O
O	O	O	O	∢
TGACTCTCCCCGA C CCGTCCCACCAI CTJGGTCTCCACA GCACTCCCGACA	TCCGCAAGGCCTT CCTGAAGATCCTI C/TCACTGCTGAC TCTGCTGCCTGCC	TCCTCGTCGCCAC C ACTGGTCATGCC C/AJTGGGTTGTCT ACCTGGAGGTGG	TTGCTCTTTGCTG GTTCCCTCTTCA[C //ITTAAGCCGTAT ATTGAAGAAAACT G	TATTGAAGAAAAC TGTGTATAACGAĮA /GJATGGACAAGAA CCGATGTGAATTA C
1278	1662	909	1471	1507
cg41084924 1278	cg41084924	cg41084924	cg43985000	cg43985000
118	119	120	121	122

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5.00E-217	3.00E-212)
Human Gene SWISSPROT- ID:P30989 NEUROTENSIN RECEPTOR TYPE 1 (NT-R-1) (HIGH-AFFINITY LEVOCABASTINE- INSENSITIVE NEUROTENSIN RECEPTOR) (NTRH) - HOMO SAPIENS (HUMAN), 418 aa.	Human Gene SWISSNEW- ID:P32247 BOMBESIN RECEPTOR SUBTYPE-3 (BRS-3) - HOMO SAPIENS (HUMAN), 399 aa. pcls:SWISSPROT-ID:P32247 BOMBESIN RECEPTOR SUBTYPE- 3 (BRS-3) - HOMO SAPIENS (HUMAN), 399 aa. pcls:TREMBLNEW-ID:E1240254 BOMBESIN RECEPTOR SUBTYPE- 3 (UTERINE BOMBESIN RECEPTOR, BRS-3) - HOMO SAPIENS (HUMAN), 399 aa.
tm7	tm7
Silent- tm7	SILENT- CODING
Lys	<u>></u>
Lys	ŗ.
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ACGTGAACACCG G ACATCTACTCCAA[G/A]GTGCTGGTGA CCGCCGTGTACC TGG	ATTCCTTGATTGC C TAGGACCCTTTA[C/TJAAAAGCACCC TGAACATACCTAC TG
561	1263
cg44930578 561	cg3003519
123	124

×	12 (14q32.1)	19 (19q13.3)	19 (19q13.3)
3.00E-212 X	9.00E-211	8.30E-208	8.30E-208
Human Gene SWISSNEW- ID:P32247 BOMBESIN RECEPTOR SUBTYPE-3 (BRS-3) - HOMO SAPIENS (HUMAN), 399 aa. pcls:SWISSPROT-ID:P32247 BOMBESIN RECEPTOR SUBTYPE- 3 (BRS-3) - HOMO SAPIENS (HUMAN), 399 aa. pcls:TREMBLNEW-ID:E1240254 BOMBESIN RECEPTOR SUBTYPE- 3 (UTERINE BOMBESIN RECEPTOR, BRS-3) - HOMO SAPIENS (HUMAN), 399 aa.	Human Gene SWISSPROT- ID:P30411 B2 BRADYKININ RECEPTOR (BK-2 RECEPTOR) - HOMO SAPIENS (HUMAN), 391 aa.	Human Gene SWISSPROT- ID:P43119 PROSTACYCLIN RECEPTOR (PROSTANOID IP RECEPTOR) (PGI RECEPTOR) - HOMO SAPIENS (HUMAN), 386 aa.	Human Gene SWISSPROT- ID:P43119 PROSTACYCLIN RECEPTOR (PROSTANOID IP RECEPTOR) (PGI RECEPTOR) - HOMO SAPIENS (HUMAN), 386 aa.
tm7	tm7	tm7	tm7
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
<u>γ</u> ο	Tyr	Ser	Val
Gly	Tyr	Ser	\ \
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O	ပ	O	ပ
CTTATGCTGTGAT CATTTCAGTGGG[C/TATCCTTGGAA ATGCTATTCTCAT CA	TCCGAAAGAAGTC TTGGGAGGTGTA C/TJCAGGGAGTGT GCCAGAAAGGGG	AGACACCCTTTC CCAGCTCGCCTCI C/AJGGGAGGAGG GACCCAAGGGCC	GCCCTCGGCCT TCGCGGTGCTGG TIC/GJACCGGACT GGCGGCCACCGA CCTGC
711	1182	1097	272
cg3003519	cg43969010	cg43263108	cg43263108
125	126	127	128

8 (8q11.2)	8 (8q11.2)	8 (8q11.2)		1 1p36.1)
8 (8)			96	`
2.10E-204 8 (8	2.10E-204	2.10E-204	1.40E-196	2.10E-195
તં		7.	,	
Human Gene SWISSPROT- ID:P41145 KAPPA-TYPE OPIOID RECEPTOR (KOR-1) - HOMO SAPIENS (HUMAN), 380 aa.	Human Gene SWISSPROT- ID:P41145 KAPPA-TYPE OPIOID RECEPTOR (KOR-1) - HOMO SAPIENS (HUMAN), 380 aa.	Human Gene SWISSPROT- ID:P41145 KAPPA-TYPE OPIOID RECEPTOR (KOR-1) - HOMO SAPIENS (HUMAN), 380 aa.	Human Gene TREMBLNEW- ID:G2736282 G PROTEIN COUPLED RECEPTOR - HOMO SAPIENS (HUMAN), 362 aa.	Human Gene SWISSPROT- ID:P41143 DELTA-TYPE OPIOID RECEPTOR (DOR-1) - HOMO SAPIENS (HUMAN), 372 aa.
tm7	tm7	tm7	tm7	tm7
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Ala	<u>=</u>	Pro	Ser	Ö N
Ala	<u>=</u>	Pro	Ser	Gly
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CCAGACTGGTCCT A GGTGGTGGTGGC[A/G]GTCTTCGTCG TCTGCTGGACTCC CA	CAGCACTCACCAT GGAATCCCCGATI C/TJCAGATCTTCC GCGGGGAGCCGG GCCGGGAGCCGG	CGATCCAGATCTT CCGCGGGGAGCC [G/T]GGCCCTACC TGCGCCCGAGC	TGGATCTGCACCT CTTCGACTACTC[A /C]GAGCCAGGGA ACTTCTCGGACAT CA	CGCTGCACCTGT GCATCGCGCTGG G[C/T]TACGCCAAT AGCAGCCTCAAC CCCG
1220	392	413	155	1154
cg43267238 1220	cg43267238	cg43267238	cg43264978	cg3001696
129	130	131	132	133

1 (1p36.1)	1 (1p31.2)	~		
2.10E-195	3.10E-194	1.10E-173	2.50E-160	2.50E-160
Human Gene SWISSPROT- ID:P41143 DELTA-TYPE OPIOID RECEPTOR (DOR-1) - HOMO SAPIENS (HUMAN), 372 aa.	Human Gene SWISSPROT- ID:P43115 PROSTAGLANDIN E2 RECEPTOR, EP3 SUBTYPE (PROSTANOID EP3 RECEPTOR) (PGE RECEPTOR, EP3 SUBTYPE) - HOMO SAPIENS (HUMAN), 390 aa.	Human Gene SWISSPROT- ID:P30542 ADENOSINE A1 RECEPTOR - HOMO SAPIENS (HUMAN), 326 aa.	Human Gene TREMBLNEW- ID:E1246031 OLFACTORY RECEPTOR - HOMO SAPIËNS (HUMAN), 312 aa.	Human Gene TREMBLNEW- ID:E1246031 OLFACTORY RECEPTOR - HOMO SAPIENS (HUMAN), 312 aa.
tm7	tm7	tm7	tm7	tm7
SILENT. CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Gly	Leu	Val	Тh	Gly
Gly	Leu	\ \ 	Ĕ	Gly
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ပ	O	O	⋖	├
TGGCTGTGACCC GTCCCCGGGACG G[G/T]GCAGTGGT GTGCATGCTCCA GTGCATGCTCCA	TGGCCTTCCCGAT CACCATGCTGCT[C/GJACTGGTTTCG TGGCAACGCAC TGG	GGGATGCCACCT TCTGCTTCATCGT[C/GJTCGCTGGCG GTGGCTGATGTG GCCG	CCATCTCCTTCTG TGGCTGTCTCAC AGJCAGATGTATT TCGTTTTCATGTT CG	GGTGGAAAGCCT TCTCCACCTGTGG [T/C]TCTCACCTGG CTGTGGTTCTCCT CT
815	407	347	358	787
cg3001696	cg42704646	cg43326635	cg3003708	cg3003708
134	135	136	137	138

2.50E-160	1.90E-153	2.10E-67	2.10E-67	2.10E-67
Human Gene TREMBLNEW- ID:E1246031 OLFACTORY RECEPTOR - HOMO SAPIENS (HUMAN), 312 aa.	Human Gene SWISSPROT- ID:Q15062 OLFACTORY RECEPTOR-LIKE PROTEIN FAT11 - HOMO SAPIENS (HUMAN), 316 aa.	Human Gene Similar to SWISSPROT-ID:P30975 TACHYKININ-LIKE PEPTIDES RECEPTOR 99D (DTKR) - DROSOPHILA MELANOGASTER (FRUIT FLY), 519 aa.	Human Gene Similar to SWISSPROT-ID:P30975 TACHYKININ-LIKE PEPTIDES RECEPTOR 99D (DTKR) - DROSOPHILA MELANOGASTER (FRUIT FLY), 519 aa.	Human Gene Similar to SWISSPROT-ID:P30975 TACHYKININ-LIKE PEPTIDES RECEPTOR 99D (DTKR) - DROSOPHILA MELANOGASTER (FRUIT FLY), 519 aa.
tm7	tm7	tm7	tm7	tm7
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Phe	Ser	nen	E S	<u>-</u> 9
Phe	Ser	Leu	E ±	u U
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ACAGCACCATCAT TGCTGTGTATTIT /CJAACCCTCTGTC CTCCCACTCAGCT G	ACTCTCCAATGTA CTTTTCCTCTC[C /IJAACCTCTCCTT CTTGGACCTCTGC T	GACATCAGGCGC ACGGTGCCAACC T[C/G]CGCCATCT GCAGGCCAAGAA GAAGT	AGGCGCACGGTG CCAACCTCCGCC A[T/C]CTGCAGGC CAAGAAGAAGTTT GTGA	CAGCCTTCTCCAT GCCCAGCTGGCA[GAJCTGGCACTGT GGCCACCAGCCT ACC
841	537	717	723	96
cg3003708	cg36729339	cg38841806	cg38841806	cg38841806
139	140	141	142	143

5 (5q32)	5 (5q32)	3 (3q25)	15
2.00E-58	2.00E-58	2.20E-207 3 (3q25)	9.00E-179
Human Gene Similar to SWISSPROT-ID:Q24563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	Human Gene Similar to SWISSPROT-ID:Q24563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	Human Gene SWISSPROT- ID:P26022 PENTAXIN-RELATED PROTEIN PTX3 PRECURSOR (TUMOR NECROSIS FACTOR- INDUCIBLE PROTEIN TSG-14) - HOMO SAPIENS (HUMAN), 381 aa.	transcriptfac Human Gene SWISSPROT- ID:Q06545 GA BINDING PROTEIN BETA-2 CHAIN (GABP-BETA-2 SUBUNIT) (TRANSCRIPTION FACTOR E4TF1-47) (GAPBP2) - HOMO SAPIENS (HUMAN), 347 aa.
tm7	tm7	th T	transcriptfac tor
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
ren	Arg	P.O.	Lys
ne _T	Arg	Pro	Lys
A	4	⊢	ව
ව	O	∢	⋖
CCTGTGCTGATCT G GGTCATGGGCCT[G/A]GCAGTGGTG CCCTTTGGGGCC GCCC	CTTGCCCATTCAG C ATGCACTGGTAC! C/AJGGGCCACCC ACCAGGAAGCCA	TTGGAAGCGTGC ATCCAGTGAGACC [A/TJATGAGGCTTG AGTCTTTTAGTGC CT	GTGTGAGCAGAG ATGCCAGAACCAA [A/G]GTGGACCGA ACACCATTACATA TGG
1966	2237	687	376
cg43040273 1966	cg43040273 2237	cg43336100	cg21646034
144	145	146	147

7-	9 (9q34)
5.30E-245	6.50E-192 9 (9q34)
Human Gene SWISSPROT- ID:P39656 DOLICHYL- DIPHOSPHOOLIGOSACCHARIDE PROTEIN GLYCOSYLTRANSFERASE 48 KD SUBUNIT PRECURSOR (EC 2.4.1.119) (OLIGOSACCHARYL TRANSFERASE 48 KD SUBUNIT) (DDOST 48 KD SUBUNIT) (KIAA0115) (HA0643) - HOMO SAPIENS (HUMAN), 456 aa.	Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (A TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B SAPIENS (HUMAN), 354 aa.
transferase	transferase
SILENT- CODING	SILENT- CODING
<u>Gly</u>	Thr
<u>^</u> io	Thr
ပ	ပ
⋖	⋖
TGGCAGCTACCA / GCACACTGCCTC C[A/G]CCGTCAAT AAAGGCACTGATG GTCT	TGGCTCCCATTGT A CTGGGAGGGCAC[A/G]TTCAACATCG ACATCCTCAACGA GC GC
	294
cg43916882 1608	cg2537639
44 8	149

9 (9q34)
6.50E-192 9 (9q34)
SILENT- transferase Human Gene SWISSPROT- CODING FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (NAGAT) - HOMO SAPIENS (HUMAN), 354 aa.
transferase
CODING CODING
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ACGTGGGCGTGG G AGATCCTGACTCC [G/A]CTGTTCGGC ACCTGCACCCC GGCT
678
cg2537639
151

9 (9q34)	
6.50E-192 9 (9q34)	
SILENT- transferase Human Gene SWISSPROT- CODING FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B SAPIENS (HUMAN), 354 aa.	
transferase	
SILENT- CODING	
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O	
GGCCCAGTCCC C AGGCCTACATCCC IC/JAAGGACGAG GGCGATTTCTACT ACC	
768	
cg2537639	
152	

9 (9q34)	16
6.50E-192 9 (9q34)	1.60E-117 16
Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B SAPIENS (HUMAN), 354 aa.	Human Gene Homologous to SWISSPROT-ID:P30711 GLUTATHIONE S-TRANSFERASE THETA 1 (EC 2.5.1.18) (CLASS- THETA) - HOMO SAPIENS (HUMAN), 239 aa.
transferase	transferase
SILENT- CODING	SILENT- CODING
Leu	\ \ \
Leu	Val
∢	U
O	4
ACGAGAGCCACC TGAACAAGTACCT [G/A]CTGCGCCAC AAACCCACCAAG GTGC	GGGGAGATACTG A GCTCACCCAGGA A A/CJACAGGGAA CATCACCTTATGC CACC
927	732
cg2537639	cg44000740
153	154

က	5 (5p15.3)		
13		1.60E-259 1	4.40E-241
Human Gene SWISSPROT- ID: P30825 HIGH-AFFINITY CATIONIC AMINO ACID TRANSPORTER-1 (CAT-1) (CAT1) (SYSTEM Y+ BASIC AMINO ACID TRANSPORTER) (ECOTROPIC RETROVIRAL LEUKEMIA RECEPTOR HOMOLOG) (ERR) (ECOTROPIC RETROVIRUS RECEPTOR HOMOLOG) - HOMO SAPIENS (HUMAN), 629 aa.	Human Gene SWISSPROT- ID:Q01959 SODIUM-DEPENDENT DOPAMINE TRANSPORTER (DA TRANSPORTER) (DAT) - HOMO SAPIENS (HUMAN), 620 aa.	Human Gene SWISSPROT- ID:P11166 GLUCOSE TRANSPORTER TYPE 1, ERYTHROCYTE/BRAIN - HOMO SAPIENS (HUMAN), 492 aa.	Human Gene SPTREMBL- ID:Q14728 TETRACYCLINE TRANSPORTER-LIKE PROTEIN MRNA - HOMO SAPIENS (HUMAN), 455 aa.
transport	transport	transport	transport
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Cys	Ser	Asp	Pro
Cys	Ser	Asp	Pro
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U	∢	9	O
ACGCAGTGGCCG TGGGCTCCTCT GC/TGCTCTTTCC GCCAGTCTTCTAG GTT	CCATCGCCACGC TCCCTCTGTCCTC [A/G]GCCTGGGCC GTGTCTTCTCA TCA	GATGGAACAGCT CCTCGGGTGTCTT [G/A]TCACTTTGGC TGGCTCCCCCCT	GCGGCTGCTGGT GGATGGGTGGGC G[C/G]GGGGTGCA GCCTCCACCCCC
1185	1347	1719	1656
cg38869466	cg40351913	cg43964039	cg43992017
155	156	157	158

	10	(C)		2 (2q34)
3	9	<u>6</u>	-	2
0	0	0	0	0
UNCLASSI Human Gene SWISSNEW- FIED ACC:Q15031 PROBABLE LEUCYL- TRNA SYNTHETASE, MITOCHONDRIAL PRECURSOR (EC 6.1.1.4) (LEUCINETRNA LIGASE) (LEURS) (KIAA0028) - Homo sapiens (Human), 903 aa.	Human Gene SPTREMBL- ACC:Q16084 P130 - HOMO SAPIENS (HUMAN), 1139 aa.	Human Gene SPTREMBL- ACC:Q16084 P130 - HOMO SAPIENS (HUMAN), 1139 aa.	Human Gene SWISSPROT- ACC:P42694 HYPOTHETICAL PROTEIN KIAA0054 - Homo sapiens (Human), 1942 aa.	Human Gene REMTREMBL- ACC:E1296438 SEQUENCE 28 FROM PATENT W09727323 - UNIDENTIFIED, 1829 aa.
UNCLASSI	UNCLASSI	UNCLASSI	UNCLASSI	UNCLASSI FIED
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
ren	Arg	Ala	Sig.	Ala
Leu	Arg	Ala	Gly	Ala
<u> </u>	O	-	<u> </u>	⋖
U	ပ	U	O	—
CGCCTGTAATGG CTGTGAACATGCT [C/T]ACCCAGCAG GAGGTCCCTGTC GTTA	CATTGACTAGGG GCTGTGGGGGCA T[C/G]CGCCCAGG TGTCCCTCCATCA GAGG	AGCAGGCCAAGA GAGATCTGTGGAA [C/T]GCATCTTGTT CCAGAATACCAGA TA	CGCTGGCATAGG ACATGGCGGGCT TIG/TJCCCCCCGC AGAGCTCTGGGG	AAATAACAAGGCA TTGAAGAATGGC[TAJGACGAGCGG AAAGACGAAGGA AAGG
1238	2875	3385	517	254
cg43948629	cg43955093	cg43955093	cg43055918	cg43974592
159	160	161	162	163

22 (22q13.1)	3 (3q21)	7 (7p15)	
0	0	0	0
UNCLASSI Human Gene SWISSPROT- FIED ACC:P13866 SODIUM/GLUCOSE COTRANSPORTER 1 (NA(+)/GLUCOSE COTRANSPORTER 1) (HIGH AFFINITY SODIUM-GLUCOSE COTRANSPORTER) - Homo sapiens (Human), 664 aa.	Human Gene SWISSNEW- ACC:P00450 CERULOPLASMIN PRECURSOR (EC 1.16.3.1) (FERROXIDASE) - Homo sapiens (Human), 1065 aa.	Human Gene SWISSPROT- ACC:P41250 GLYCYL-TRNA SYNTHETASE (EC 6.1.1.14) (GLYCINETRNA LIGASE) (GLYRS) - Homo sapiens (Human), 685 aa.	Human Gene SWISSPROT- ACC:P02771 ALPHA- FETOPROTEIN PRECURSOR (ALPHA-FETOGLOBULIN) (ALPHA- 1- FETOPROTEIN) - Homo sapiens (Human), 609 aa.
UNCLASSI	UNCLASSI	UNCLASSI FIED	UNCLASSI FIED
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Asp	Lys	Ala	ng
Asp	Lys	Ala	nio Oin
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O	∢		⋖
AAGGACGCAACG CTGCCACCATGG A[C/T]AGTAGCAC CTGGAGCCCCAA GACCA	TGAAAGTATTCAA TCCCAGAAGGAA[A/G CTGGAATTG CCCTTCTGTTTCT AG	GCTGGCGCACTG CTAGCCTCAGAG G[T/A]GCCAGCAC CTCCTCAGCCCC CGCGC	AAAACCAGCTACC A TGCCTTTCTGGA[A/GJGAACTTTGCC ATGAGAAAGAAAT TT
206	2757	2472	481
cg43956384	cg44025634	cg43940037	cg44024279 481
164	165	166	167

CATGAGITITIGAT CCCAGCICTICII C/ITCCCIGGCIT TCTGGGCCATITC TC		
C()1		ACC:P51854 TRANSKETOLASE 2 (EC 2.2.1.1) (TK 2) (TRANSKETOLASE RELATED PROTEIN) - Homo sapiens (Human), 557 aa. (SSI Human Gene SWISSPROT- 3.90E-257
TCAACACCTACGT G T CCACTTCCAAGG G T CCACTTCCAAGG G T CCTTCTCCTGCT G T CCTTCTCCTGCT G G CCTTCTCCTGCT G G CCTTCTCCTGCT G G CCTTCTCCTGCT G CCTTCTCTCTGCT G CCTTCTCTCTGCT G CCTTCTCTCTGCT G CCTTCTCCTGCT G CCTTCTCTCTGCT G CCTTCTCTCTGCT G CCTTCTCTCTGCT G CCTTCTCTCTGCT G CCTTCTCTCTCTGCT G CCTTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTCTC		ACC:P01019 ANGIOTENSINOGEN PRECURSOR - Homo sapiens (Human), 485 aa.
TGGCTTGCACAAA A TTGCTTGAAGAC[A/TJCGATCCATGT AAGTGGACTGTCT TG	Arg SILENT- UNCLASSI CODING FIED	Human Gene SPTREMBL- ACC:043411 HYPOTHETICAL 49.3 KD PROTEIN - HOMO SAPIENS (HUMAN), 442 aa (fragment).
CTGGCCAGCTGC C G CCTCACAGTAGTT [C/G]CCGTAGTAG CCGGTGGGTGCT ATGA	GIY GIY SILENT- UNCLASSI CODING FIED	ASSI Human Gene SWISSPROT- ACC:P09529 INHIBIN BETA B CHAIN PRECURSOR (ACTIVIN BETA-B CHAIN) - Homo sapiens (Human), 407 aa.

2 (2cen)	12	12	11 (11p15.5)
	2.40E-225	2.40E-225	2.10E-224 11
UNCLASSI Human Gene SWISSPROT- ACC:P09529 INHIBIN BETA B CHAIN PRECURSOR (ACTIVIN BETA-B CHAIN) - Homo sapiens (Human), 407 aa.	Human Gene SWISSPROT-ACC:P29080 (2'-5')OLIGOADENYLATE SYNTHETASE 1B (EC 2.7.7) ((2-5')OLIGO(A) SYNTHETASE 1B) (2-5A SYNTHETASE 1B) - Mus musculus (Mouse), 414 aa.	Human Gene SWISSPROT- ACC:P29080 (2'- 5)OLIGOADENYLATE SYNTHETASE 1B (EC 2.7.7) ((2- 5)OLIGO(A) SYNTHETASE 1B) (2- 5A SYNTHETASE 1B) - Mus musculus (Mouse), 414 aa.	Human Gene SWISSPROT- ACC:P04177 TYROSINE 3- MONOOXYGENASE (EC 1.14.16.2) (TYROSINE 3-HYDROXYLASE) (TH) - Rattus norvegicus (Rat), 498 aa.
UNCLASSI	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Arg	G	년	Thr
Arg	년 -	<u>u</u>	Thr
—	F	F	U
O	U	O	O
GCCGAGCCTGCA CCACCACAAAGG G[C/T]CGGTGCGA CTCTTCGCCTGG	CATAGAAGGCCA GGAGTCAGGAGA C[C/T]TGGGTTCT GTCCTGGATTATA CACC	GGAGTCAGGAGA CCTGGGTTCTGTC [C/I]TGGATTATAC ACCAGCTCACTGA GG	CCATGCCCACCC CCGACGCCACCA C[G/C]CCACAGGC CAAGGGCTTCCG CAGGG
2354	256	268	53
cg42913861	cg43929685	cg43929685	cg43918561
173	174	175	176

8 (8p12)	-	19 (19q13)	19 (19q13)
3.90E-218 8 (8p12)	4.90E-211	1.30E-210 19 (19	1.30E-210
UNCLASSI Human Gene SWISSPROT-ACC:P14902 INDOLEAMINE 2,3-DIOXYGENASE (EC 1.13.11.42) (IDO) (INDOLEAMINE-PYRROLE 2,3-DIOXYGENASE) - Homo sapiens (Human), 403 aa.	Human Gene SPTREMBL- ACC:Q99816 TUMOR SUSCEPTIBILITY PROTEIN - HOMO SAPIENS (HUMAN), 390 aa.	Human Gene SWISSPROT- ACC:015382 BRANCHED-CHAIN AMINO ACID AMINOTRANSFERASE, MITOCHONDRIAL PRECURSOR (EC 2.6.1.42) (BCAT(M)) - Homo sapiens (Human), 392 aa.	Human Gene SWISSPROT- ACC:O15382 BRANCHED-CHAIN AMINO ACID AMINOTRANSFERASE, MITOCHONDRIAL PRECURSOR (EC 2.6.1.42) (BCAT(M)) - Homo sapiens (Human), 392 aa.
UNCLASSI FIED	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT. CODING
Val	<u>e</u>	ren	<u>ਲ</u>
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ATTTAATGAATTTC A CTGAAGACTGT[A/ GJAGAAGTACAAC TGAGAATCCCTT T	AAAACAATGATAT CGATGAAGTTAT[C/TJATTCCCACAG CTCCCTTATACAA AC	CACCATGAAGCA GTTGCTGCGGGC C[C/T]TGGAGGAG GGCCGCGTGCGG GAAGT	TCCTGTACAAAGA CAGGAACCTCCA C/TATTCCCACCA TGGAAATGGGC CTG
1885	1146	979	1074
cg42343176 1885	cg43956382	cg43984681	cg43984681
177	178	179	180

_	22	G.
6.20E-204 1	1.90E-200 22	5.60E-191 9
SILENT- UNCLASSI Human Gene SPTREMBL- CODING FIED ACC:P78545 ESE-1B - HOMO SAPIENS (HUMAN), 371 aa.	Human Gene SPTREMBL- ACC:O60704 TYROSYLPROTEIN SULFOTRANSFERASE-2 - HOMO SAPIENS (HUMAN), 377 aa.	UNCLASSI Human Gene SWISSNEW-ACC:Q03385 GUANINE NUCLEOTIDE DISSOCIATION STIMULATOR RALGDS FORM A (RALGEF) - Mus musculus (Mouse),
UNCLASSI	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT- CODING	SILENT- CODING
Pro	Leu	ren
Pro	neŋ	ren Fen
O	V	ပ
d	ල	U
CTGCGGTGGAGA A CGTCAGAGCTGC C[A/G]GGGGAGGG GGCTCCTGCGCCC ACAGC	ACCAGCTGCTCGT G AGTACACAGGCA[G/A]GCACTTCTCC TTGCCTACCTCCA	CTACCGCCAACTA C TGACTTTGTCCT[C /G]AAGAAGCGGA CCTTCACCAAGG GAG
	888	1114
cg43950996 1762	cg44024506	cg43980381
181	182	183

	15	9 (9q22.2)
2.00E-189	1.40E-188	3.50E-178 9 (9)
Human Gene SWISSPROT- ACC:Q10981 GALACTOSIDE 2-L- FUCOSYLTRANSFERASE 2 (EC 2.4.1.69) (GDP-L-FUCOSE:BETA- D- GALACTOSIDE 2-ALPHA-L- FUCOSYLTRANSFERASE 2) (ALPHA(1,2)FT 2) (FUCOSYLTRANSFERASE 2) (FUCOSYLTRANSFERASE 2) (SECRETOR BLOOD GROUP ALPHA-2- FUCOSYLTRANSFERASE) (SECRETOR FACTOR) (SE) - Homo sapiens (Human), 343 aa.	Human Gene SWISSPROT- ACC:P09471 GUANINE NUCLEOTIDE-BINDING PROTEIN G(O), ALPHA SUBUNIT 1 - Homo sapiens (Human), 353 aa.	Human Gene SWISSPROT- ACC:P09467 FRUCTOSE-1,6- BISPHOSPHATASE (EC 3.1.3.11) (D-FRUCTOSE-1,6- BISPHOSPHATE 1- PHOSPHOHYDROLASE) (FBPASE) - Homo sapiens (Human), 337 aa.
UNCLASSI	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT- CODING	SILENT- CODING
Asn	Val	Ala
Asn	Val	Ala
⊢	H	⋖
C		O
TCCCCTGGCAGA (ACTACCACCTGAA (C/T)GACTGGATG GAGGAGAATAC CGCC	ACATCCAGGTGGT (GTTCGACGCGT[CT]ACCGACATCATCATTGCCAACAACAACAACAACAACAACAACAACAACAACAACA	CAGTGACGGCAG (GGTCAAAGTCCTT [G/A]GCGTAGCCC TCGTTAAGGCTGT AGA
501	1497	615
cg42650960	cg43249389	cg43946951
184	185	186

16 (16p13.1 1)	8 (8p23.1)	22		
	5.40E-157		9.60E-148	9.60E-148
Human Gene SWISSPROT- ACC:Q14894 MU-CRYSTALLIN HOMOLOG (NADP-REGULATED THYROID-HORMONE BINDING PROTEIN) - Homo sapiens (Human), 314 aa.	Human Gene SWISSNEW- ACC:P11245 ARYLAMINE N- ACETYLTRANSFERASE, POLYMORPHIC (EC 2.3.1.5) (PNAT) (NAT-2) (ARYLAMINE ACETYLASE) - Homo sapiens (Human), 290 aa.	Human Gene SPTREMBL- ACC:Q15729 THYROTROPH EMBRYONIC FACTOR - HOMO SAPIENS (HUMAN), 303 aa.	Human Gene Homologous to SWISSNEW-ACC:Q12846 SYNTAXIN 4 - Homo sapiens (Human), 297 aa.	Human Gene Homologous to SWISSNEW-ACC:Q12846 SYNTAXIN 4 - Homo sapiens (Human), 297 aa.
UNCLASSI	UNCLASSI	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT-CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Thr	Tyr	걘	Arg	Gly
Thr	Tyr	Thr	Arg	Gly
U	H	—	I	ပ
O	U	O	ග	9
AACCAGCCCACT GTGAGAAGACCA C[G/C]GTGTTCAA GTCTTTGGGAATG GCAG	CCACAATGTTAGG AGGGTATTTTA[C MJATCCCTCCAGT TAACAAATACAGC A	CTGCCATCTTTCA GCCCTCTGAAACI C/TJGTGTCCAGCA CAGAATCTTCCCT GG	GCGCTTCCCAGG TCCGGACAATTCG [G/T]CAGACTATTG TCAAACTGGGGAA TA	GGCAGCTGAAGA TCACCAATGCTGG [G/C]ATGGTGTCT GATGAGGAGTTG GAGC
1054	482	499	350	701
cg43248117 1054	cg44027049	cg43982075	cg43942977	cg43942977
187	188	189	190	191

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	æ	ω	19
-148	-145	-145	2.80E-144 19
9.60E-148	5.10E-145	5.10E-145	2.80E
Human Gene Homologous to SWISSNEW-ACC:Q12846 SYNTAXIN 4 - Homo sapiens (Human), 297 aa.	Human Gene Homologous to SWISSNEW-ACC:P29218 MYO- INOSITOL-1(OR 4)- MONOPHOSPHATASE (EC 3.1.3.25) (IMP) (INOSITOL MONOPHOSPHATASE) (LITHIUM- SENSITIVE MYO-INOSITOL MONOPHOSPHATASE A1) - Homo sapiens (Human), 277 aa.	Human Gene Homologous to SWISSNEW-ACC:P29218 MYO- INOSITOL-1(OR 4)- MONOPHOSPHATASE (EC 3.1.3.25) (IMP) (INOSITOL MONOPHOSPHATASE) (LITHIUM- SENSITIVE MYO-INOSITOL MONOPHOSPHATASE A1) - Homo sapiens (Human), 277 aa.	Human Gene Homologous to SWISSPROT-ACC:P29692 ELONGATION FACTOR 1-DELTA (EF-1-DELTA) - Homo sapiens (Human), 281 aa.
UNCLASSI FIED	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Leu	Gly	Ser	Ala
ren	Gly	Ser	Ala
—	O	 	O
Ø		U	∢
GCGAGGTGTTTGT G GTCCAATATCCT GTJAAGGACACGC AGGTGACTCGAC	TGTACACTGCCAG AAAAGGAAAAGG[T/G]GCCTTTTGTA ATGGTCAAAAACT AC	TCTTGGTGACTGA GTTGGGCTCTTC[C/T]AGAACACCAG AGACTGTGAGAAT GG	TAGAGCGCACAC AGGCCTCCAGGT GIAGGCCATGTC CGTCTCATCATCC CAAG
773	753	837	321
cg43942977 773	cg43985220	cg43985220	cg43946394
192	193	194	195

8 (8q22)	2 (2p13)	20	19 (19q13.4)	6
6.90E-141 8 (8q22)			2.10E-100	6.80E-95
Human Gene Homologous to SWISSPROT-ACC:P00915 CARBONIC ANHYDRASE I (EC 4.2.1.1) (CARBONATE DEHYDRATASE I) - Homo sapiens (Human), 260 aa.	Human Gene Homologous to SWISSPROT-ACC:Q05195 MAD PROTEIN (MAX DIMERIZER) - Homo sapiens (Human), 221 aa.	Human Gene Homologous to TREMBLNEW-ACC:AAD43195 PEROXISOMAL MEMBRANE PROTEIN PMP 24 - HOMO SAPIENS (HUMAN), 212 aa.	Human Gene Similar to TREMBLNEW-ACC:BAA13472 CD89_U08 - HOMO SAPIENS (HUMĀN), 191 aa.	Human Gene Similar to TREMBLNEW-ACC:CAB43107 PRENYLATED RAB ACCEPTOR 1 (PRA1) - HOMO SAPIENS (HUMAN), 185 aa.
UNCLASSI FIED	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI	UNCLASSI FIED
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Phe	Leu	Val	Arg	Pro
Phe	Leu	Val	Arg	Pro
<u> </u>	o	U	O	
ပ	F	- -	V	O ,
CTGACAGCTACAG C GCTCTTTCAGTT[C //JCATTTCACTG GGGCAGTACAAAT G	AGAAGTTGAAGG GGCTGGTGCCAC T[T/G]GGACCCGA ATCAAGTCGACAC ACTA	TGGGTTCAGGGA TGTAGCCCTTCTC [I/C]ACAGCCAGG CGGCTCAGGGCA	GCCAATATAGGAT AGGGCACTACAGI AGITTCCGGTACA GTGACACCCTGG AGC	ACGGGGAGGAGC TGCAGATGGAAC C[C/T]GTGTGAGG TGTCTTCTGGGAC CTGC
1329	735	998	402	629
cg43119818 1329	cg43118279	cg43325007	cg39524111	cg43280516
196	197	198	199	200

Ξ		9 (12q23)		
	1.30E-89	3.80E-85		5.60E-68
Human Gene Similar to SPTREMBL- 5.10E-90 ACC:014803 BCL-X/BCL-2 BINDING PROTEIN - HOMO SAPIENS (HUMAN), 168 aa (fragment).	Human Gene Similar to TREMBLNEW-ACC:BAA34941 HUMAN CMAP - HOMO SAPIENS (HUMAN), 167 aa.	Human Gene Similar to SWISSPROT-ACC:P09496 CLATHRIN LIGHT CHAIN A (BRAIN AND LYMPHOCYTE LCA) - Homo sapiens (Human), 248 aa.	Human Gene Similar to SPTREMBL-ACC:000496 IPL (IPL) - HOMO SAPIENS (HUMAN), 152 aa.	Human Gene Similar to REMTREMBL-ACC:G36907 T-CELL RECEPTOR ALPHA-CHAIN HAP58 V(A)10.1-J(A)T - HOMO SAPIENS (HUMAN), 135 aa (fragment).
UNCLASSI	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI	UNCLASSI
SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING	SILENT- CODING
Arg	Leu	Pro	Leu	Arg
Arg	Leu	Pro	Leu	Arg
4	U	U		9
ග	ပ	<u></u>	O	⋖
AGAGGTTGGGGG GCGCCGAGCGCG A[G/A]CGGCCCCG AAAGGGGCTGGG	TAGTGAAAGGCCT GAAATATATGCT[G /C]GAGGTGGAAAT TGGCAGAACTACC T	CTCCATCAACAGC ATCCGGACTGCA[T/C]GGCGGCTCG CCGTGCGGCTGG	CGACGAGGTGCT ACGCGAGGGCGA GC/TJTGGAGAAG CGCAGCGACAGC	TTTTTCCAGCTT ACAATGGTACAG[A/G]CAGGAGGCCT GGGGAAGGTCCT GTCC
871	682	915	136	162
cg43963913 871	cg40262905	cg43918168	cg43259701	cg1527767
201	202	203	204	205

11 (11p15.2)	7 (7q35)		-	17
	8.50E-56	1.60E-54	2.00E-54	0
UNCLASSI Human Gene Similar to SWISSNEW- 5.10E-58 FIED ACC:P06881 CALCITONIN GENE- RELATED PEPTIDE I PRECURSOR (CGRP-I) (ALPHA-TYPE CGRP) - Homo sapiens (Human), 128 aa.	Human Gene Similar to REMTREMBL-ACC:D1002898 T- CELL RECEPTOR BETA-CHAIN V REGION - HOMO SAPIENS (HUMAN), 112 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).	Human Gene Similar to SWISSNEW- 2.00E-54 ACC:P47992 LYMPHOTACTIN PRECURSOR (CYTOKINE SCM-1) (ATAC) (LYMPHOTAXIN) (SCM-1- ALPHA) - Homo sapiens (Human),	Human Gene SPTREMBL- ID:Q93050 VACUOLAR-TYPE H(+)- ATPASE 115 KDA SUBUNIT - HOMO SAPIENS (HUMAN), 831 aa.
UNCLASSI	UNCLASSI FIED	UNCLASSI	UNCLASSI	ATPase_as sociated
SILENT- CODING	SILENT- CODING	SILENT. CODING	SILENT- CODING	SILENT- ATPase NONCODI sociated NG
Thr	Fen	Thr	Th.	
1	Leu	Thr	Thr	
F	O	O	<u>o</u>	gap
O	—	 -	A	o
AGAAGAGAGCCT GTGACACTGCCA C[C/T]TGTGTGACT CATCGCTGGCA GGCT	TCATCCTGAGTTC TAAGAAGCTCCT[T /C]CTCAGTGACTC TGGCTTCTATCTC T	CTCTGGTTGTCCA CGAGGGAGACACI TCJGTAACTCTCA ATTGCAGTTATGA AG	AAGTCTGTGCTGA TCCACAAGCCAC[A/G]TGGGTGAGA GACGTGGTCAGG AGCA	AGGGAGGCGGGG G AGGGTAGCATGG G[G/gap]CACACGG CCCTCACAGGGA
316	300	317	249	1571
cg40968986 316	cg42550133	cg2526759	cg41664708	cg43300673
206	207	208	209	210

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_	9.40E-58	0	0	0
Human Gene Homologous to SPTREMBL-ID:Q18788 C52E4.5 - CAENORHABDITIS ELEGANS, 590 aa.	Human Gene Similar to SPTREMBL- ID:Q15332 GAMMA SUBUNIT OF SODIUM POTASSIUM ATPASE LIKE - HOMO SAPIENS (HUMAN), 126 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.
ATPase_as sociated	SILENT- ATPase_as NONCODI sociated NG	cadherin	cadherin	cadherin
SILENT- ATPase NONCODI sociated NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
∢	U	—	—	O
gap	٥	g	₀	gap
AGTTGAAATCAGA gap GAGGAATAAAAA[g ap/A]GACATTTTAT ATTTTATTCTGCT CC	TAAGCATGAGGTG A GCACGAGGCAGGI ACJGTTGGCGATG CCACCTGGGGGT CAC	GGTCCCCTTGCTT TATCCCAAGCTC G/TJGAGGGACGC AGCCTGGCATGG CTCT	GTCCCTTGCTTT ATCCCAAGCTCGI G/TJAGGGACGCA GCCTGGCATGGC TCTG	CTTTATCCCAAGC TCGGAGGGACGC[gap/GJAGCCTGGC ATGGCTCTGGCCT AGCA
2570	196	909	607	615
cg43284434 2570	cg43132502	cg43931765	cg43931765	cg43931765
211	212	213	214	215

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0	0	0	0	0
Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.	Human Gene SWISSPROT- ID:P18084 INTEGRIN BETA-5 SUBUNIT PRECURSOR - HOMO SAPIENS (HUMAN), 799 aa.
cadherin	cadherin	cadherin	cadherin	cadherin
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
-	—	-	—	F
gap	gap	gap	gap	gap
TAGCAGCCAGGT GACATGGCCAGG C[gap/T]ACCTTCC TGTACAGGCACTG	GCCAGGTGACAT GGCCAGGCACCT T[gap/T]CCTGTAC AGGCACTGTGGG	AGGTGACATGGC CAGGCACCTTCCT [gap/I]GTACAGGC ACTGTGGGCTCCT GGCC	AGGTGACATGGC CAGGCACCTTCCT Igap/I]GTACAGGC ACTGTGGGCTCCT GGCC	AGGTGACATGGC CAGGCACCTTCCT Igap/TJGTACAGGC ACTGTGGGCTCCT GGCC
099	965	899	899	899
cg43931765 660	cg43931765	cg43931765	cg43931765	cg43931765
216	217	218	219	220

16	16 (16p11.2)	1 (1923)
0	0	1.00E-218 1 (1q23)
Human Gene SPTREMBL- ID:Q15065 OB-CADHERIN-1 - HOMO SAPIENS (HUMAN), 796 aa.	Human Gene SWISSPROT- ID:P20701 LEUKOCYTE ADHESION GLYCOPROTEIN LFA-1 ALPHA CHAIN PRECURSOR (LEUKOCYTE FUNCTION ASSOCIATED MOLECULE 1, ALPHA CHAIN) (CD11A) (INTEGRIN ALPHA- L) - HOMO SAPIENS (HUMAN), 1170 aa.	Human Gene SWISSPROT- ID:P14151 L-SELECTIN PRECURSOR (LYMPH NODE HOMING RECEPTOR) (LEUKOCYTE ADHESION MOLECULE-1) (LAM-1) (LEUKOCYTE SURFACE ANTIGEN LEU-8) (TQ1) (GP90-MEL) (LEUKOCYTE-ENDOTHELIAL CELL ADHESION MOLECULE 1) (LECAM1) (CD62L) - HOMO SAPIENS (HUMAN), 372 aa.
cadherin	cadherin	cadherin
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
O	—	ပ
⋖	Ø	F
AATCCACAATCGG A CATCAGGAAGCC[ACJAAGTCCCAGT GGCCATTAGGGT CCT	TCCCTATGAGCCT GCAAAGGAGACA[G/TJCCAGGAATGA GTTCCATGTTCGA GA	CAGTGCATCTGG GAAGATTTCTACC[T/C]GACCAACAGT TCCTTCAGCTTCC AT
4769	1406	1463
cg43952088 4769	cg44010957 1406	cg43956560
221	222	223

1 (1923)	1 (1q23)
1.00E-218 1 (1q23)	1.00E-218 1 (1q23)
Human Gene SWISSPROT- ID:P14151 L-SELECTIN PRECURSOR (LYMPH NODE HOMING RECEPTOR) (LEUKOCYTE ADHESION MOLECULE-1) (LAM-1) (LEUKOCYTE SURFACE ANTIGEN LEU-8) (TQ1) (GP90-MEL) (LEUKOCYTE-ENDOTHELIAL CELL ADHESION MOLECULE 1) (LECAM1) (CD62L) - HOMO SAPIENS (HUMAN), 372 aa.	Human Gene SWISSPROT- ID:P14151 L-SELECTIN PRECURSOR (LYMPH NODE HOMING RECEPTOR) (LEUKOCYTE ADHESION MOLECULE-1) (LAM-1) (LEUKOCYTE SURFACE ANTIGEN LEU-8) (TQ1) (GP90-MEL) (LEUKOCYTE-ENDOTHELIAL CELL ADHESION MOLECULE 1) (LECAM1) (CD62L) - HOMO SAPIENS (HUMAN), 372 aa.
cadherin	cadherin
SILENT- NONCODI NG	SILENT- NONCODI NG
Y	⋖
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CAACAGTTCCTTC G AGCTTCCATTTC[G /A]CCCCTCATTTA TCCCTCAACCCCC A	TGCTCTTTCC CCCTGCCCCAGA[CAJCTTTTATCCAGATCTTACCTAGATTCTA
cg43956560 1492	cg43956560 2242
224	225

_			5 (5p13)	9 (9q34.3)
4.10E-183	0	0		1.40E-104
Human Gene SWISSPROT- ID:P43235 CATHEPSIN K PRECURSOR (EC 3.4.22.38) (CATHESPIN O) (CATHEPSIN X) (CATHEPSIN O2) - HOMO SAPIENS (HUMAN), 329 aa.	Human Gene SWISSPROT- ID:P27658 COLLAGEN ALPHA 1(VIII) CHAIN PRECURSOR (ENDOTHELIAL COLLAGEN) - HOMO SAPIENS (HUMAN), 744 aa.	Human Gene SWISSPROT- ID:P27658 COLLAGEN ALPHA 1(VIII) CHAIN PRECURSOR (ENDOTHELIAL COLLAGEN) - HOMO SAPIENS (HUMAN), 744 aa.	complement Human Gene SWISSPROT- ID:P10643 COMPLEMENT COMPONENT C7 PRECURSOR - HOMO SAPIENS (HUMAN), 843 aa.	complement Human Gene Homologous to SWISSPROT-ID:P07360 COMPLEMENT C8 GAMMA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 202 aa.
cathepsin	collagen	collagen	complement	complement
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
A	O	O	ပ	ق ق
 	O	O	4	O
TGGCCACAGTGA AAAAGGTCATGG G[T/A]GGAGAGAA GCAAAGTAGGAA GGATC	ACCGCACCCTTTC CACCGGTGGGGG [C/G]CCCAGTGAA GTTTAACAAACTG CTG	CATACCACGTTCA CTGCAAGGGGGG[C/G]AACGTGTGG GTTGCTCTATTCA AGA	GAAACCCAGTAG GCTCCTGGAGGC C[A/C]TGGTCAGC TTGCTTGGAATCC AGCA	TGGTGGTGCTAC CCTTGGCCTCCCA [C/G]AGTCCTGCC ACCTGCTGCCG CCAC
428	1972	2096	2546	64
cg43264626 428	cg43011543	cg43011543	cg43933757	cg41553795
226	227	228	229	230

3 (3q26.3)	3 (3q26.3)	17 (17q11.2)
1.20E-189	1.20E-189	1.50E-107 17 (1.50E-107 (1.50E-10
Human Gene SWISSPROT- ID:P40225 THROMBOPOIETIN PRECURSOR (MEGAKARYOCYTE COLONY STIMULATING FACTOR) (C-MPL LIGAND) (ML) (MEGAKARYOCYTE GROWTH AND DEVELOPMENT FACTOR) (MGDF) - HOMO SAPIENS (HUMAN), 353 aa.	Human Gene SWISSPROT- ID:P40225 THROMBOPOIETIN PRECURSOR (MEGAKARYOCYTE COLONY STIMULATING FACTOR) (C-MPL LIGAND) (ML) (MEGAKARYOCYTE GROWTH AND DEVELOPMENT FACTOR) (MGDF) - HOMO SAPIENS (HUMAN), 353 aa.	Human Gene Homologous to SWISSPROT-ID:P09919 GRANULOCYTE COLONY- STIMULATING FACTOR PRECURSOR (G-CSF) (PLURIPOIETIN) - HOMO SAPIENS (HUMAN), 207 aa.
SILENT- csf NONCODI NG	SILENT- csf NONCODI NG	SILENT- csf NONCODI NG
SILE	N N N N N N N N N N N N N N N N N N N	NO NO NO
-	F	
O	O	U
AGCCCTTCTCCAC C CCGGATAGATTC[C/TJTCACCCTTGG CCCGCCTTTGCC CCA	ACCCGGATAGATT CCTCACCCTTGG C/TCCGCCTTTGC CCCACCCTACTCT GC	GTGCCTGGACATT TGCCTTGCTGGA[C/TJGGGGACTGG GGATGTGGGAGG GATGTGGGAGG
	179	1356
cg42542496 168	cg42542496	cg41533258
231	232	233

<u>.</u>	10
10E-77	5.80E-303
<u></u>	
Human Gene Similar to SWISSNEW- 1.10E-77 ID:P08700 INTERLEUKIN-3 PRECURSOR (IL-3) (MULTIPOTENTIAL COLONY-STIMULATING FACTOR) (HEMATOPOIETIC GROWTH FACTOR) (MCGF) - HOMO SAPIENS (HUMAN), 152 aa.jpcls:SWISSPROT-ID:P08700 INTERLEUKIN-3 PRECURSOR (IL-3) (MULTIPOTENTIAL COLONY-STIMULATING FACTOR) (HEMATOPOIETIC GROWTH FACTOR) (MCGF) - HOMO SAPIENS (HUMAN), 152 aa.	dehydrogen Human Gene SWISSPROT- ase ID:P00367 GLUTAMATE DEHYDROGENASE 1 PRECURSOR (EC 1.4.1.3) (GDH) - HOMO SAPIENS (HUMAN), 558 aa.
csf	dehydrogen ase
SILENT- NONCODI NG	SILENT- deh NONCODI ase NG
O	ပ
deb	O
ACGACTTTGAGCC gap TCGCGATCTTTIg ap/G]AGTCCAACG TCCAGCTCGTTCT CTG CTG	TGCGGCTTAAAAG G GGCAACCCGCGC[G/CJGGACCCTTCC TCCCTAGTCGCG GGG
657	225
cg2753430	cg44036323
234	235

7 (7q31)	4 (4922)	
5.10E-272 7 (7q31)	1.30E-209	0
dehydrogen Human Gene SPTREMBL- ase ID:Q14131 DIHYDROLIPOAMIDE DEHYDROGENASE - HOMO SAPIENS (HUMAN), 511 aa.	dehydrogen Human Gene SWISSNEW- ase ID:P08319 ALCOHOL DEHYDROGENASE CLASS II PI CHAIN (EC 1.1.1.) - HOMO SAPIENS (HUMAN), 391 aa.jpcls:SWISSPROT-ID:P08319 ALCOHOL DEHYDROGENASE CLASS II PI CHAIN (EC 1.1.1.) - HOMO SAPIENS (HUMAN), 391 aa.	Human Gene SWISSNEW- ID:P19838 NUCLEAR FACTOR NF- KAPPA-B P105 SUBUNIT (DNA- BINDING FACTOR KBF1) (EBP-1) [CONTAINS: NUCLEAR FACTOR NF-KAPPA-B P50 SUBUNIT]- HOMO SAPIENS (HUMAN), 969 aa. pcis:SWISSPROT-ID:P19838 NUCLEAR FACTOR NF-KAPPA-B P105 SUBUNIT (CONTAINS: NUCLEAR FACTOR NF-KAPPA-B P50 SUBUNIT) (DNA-BINDING FACTOR KBF1) (EBP-1) - HOMO SAPIENS (HUMAN), 969 aa.
dehydrogen ase	dehydrogen ase	dna_ma_bi
SILENT- deh NONCODI ase NG	SILENT. deh NONCODI ase NG	SILENT- dn NONCODI nd NG
	O	O
O	gap	deb
GAGAGACCATITA CITACATCAGTI[C //JGGTTTATAGAC ATTTGAATCATAT C	AGTTTCATTATAC (TITTCTCTCCAC) ap/GjTTTGTCTAT GTTGAAAATTTTC TG	ACAAGACAGAAG CTGAAGTGCATCC Igap/CJAAAGGTGC TCAGAGAGCCGG CCCGC
766	1995	3691
cg43918671	cg43057018	cg44005808
236	237	238

	10	9
0	1.40E-159	1.40E-159
dna_ma_bi Human Gene SWISSNEW- ID:P19838 NUCLEAR FACTOR NF- KAPPA-B P105 SUBUNIT (DNA- BINDING FACTOR KBF1) (EBP-1) [CONTAINS: NUCLEAR FACTOR NF-KAPPA-B P50 SUBUNIT]- HOMO SAPIENS (HUMAN), 969 aa. [pcis:SWISSPROT-ID:P19838 NUCLEAR FACTOR NF-KAPPA-B P105 SUBUNIT (CONTAINS: NUCLEAR FACTOR NF- KAPPA-B P50 SUBUNIT) (DNA-BINDING FACTOR KBF1) (EBP-1) - HOMO SAPIENS (HUMAN), 969 aa.	dna_rna_bi Human Gene SPTREMBL- nd ID:Q99612 DNA-BINDING PROTEIN CPBP - HOMO SAPIENS (HUMAN), 290 aa (fragment).	Human Gene SPTREMBL- ID:Q99612 DNA-BINDING PROTEIN CPBP - HOMO SAPIENS (HUMAN), 290 aa (fragment).
dna_rna_bi	dna_ma_bi nd	dna_rna_bi nd
SILENT- das NONCODI nd NG	SILENT- dra NONCODI nd NG	SILENT- NONCODI NG
တ	4	 -
gap	gap	gap
TCTTCCTTCTCA gap GCCGGCAGGCCC [gap/G]CGCCGCTT AGGAGGGAGAGC CCACC	TGGCGAGTCCAG GGTCACCCACATA [gap/A]CCATGCAC CACGGGTGCTAT GCCGC	GAGTCCAGGGTC ACCCACATACCAT [gap/T]GCACCACG GGTGCTATGCCG CTTCT
630	1244	1248
cg44005808 630	cg43956159	cg43956159
239	240	241

			1p36.13
99 10	-	10	+
1.40E-159 10	1.40E-159	1.40E-159	.30E-60
PROTEIN HUMAN),	PROTEIN HUMAN),		Human Gene Similar to SWISSNEW- 1 ID:Q02535 DNA-BINDING PROTEIN INHIBITOR ID-3 (ID-LIKE PROTEIN INHIBITOR HLH 1R21) (HELIX- LOOP-HELIX PROTEIN HEIR-1) - HOMO SAPIENS (HUMAN), 119 aa.jpcls:SWISSPROT-ID:Q02535 DNA-BINDING PROTEIN INHIBITOR ID-3 (ID-LIKE PROTEIN INHIBITOR HLH 1R21) (HELIX-LOOP-HELIX PROTEIN HEIR-1) - HOMO SAPIENS (HUMAN), 119 aa.
dna_ma_bi nd	dna_rna_bi nd	dna_rna_bi nd	SILENT- dna_rna_bi NONCODI nd_inhib NG
SILENT- drig NONCODI nd NG	SILENT- dra NONCODI nd NG	SILENT- dre NONCODI nd NG	SILENT- NONCODI NG
4	U	U	—
	65	gap	
TACCATGCACCAC GGGGGGGGGGGGGGGGGGTGTTACAGGGGGGGGGG	CCTGGAGGCAAC GTGGTAGGTAGGTAGGTAGGGTGCATGGCTGGAACGCATGGCTGGAACGCAACGCAACGCAACGCAACGCTGGAACACGCAACGCTGGAACACGCAACACACACACACACACACACACACACACACACACACAC	CAGAACGGCATG CTTTGGCTGGAAC [gap/C]ACGCATCC CTCCTTCCACGGC CGGC	CAGAGCTAGCTCT C GGCTCTTCAGGC[C/IJACAAGTTCAC AGTCCTTCGCTCC TG
1268	1342	1364	471
cg43956159	cg43956159	cg43956159	cg43971258
242	243	244	245

246	cg43971258	508	GTCCTTCGCTCCT TGAGGCACCAGGTT[TC]AGGCATTGGTGAAGGGATTTGGTGAAA		O	SILENT- dna_ma_NONCODI nd_inhib_NG	dna_rna_bi nd_inhib	Human Gene Similar to SWISSNEW- 1.30 ID:Q02535 DNA-BINDING PROTEIN INHBITOR ID-3 (ID-LIKE PROTEIN INHBITOR HLH 1R21) (HELIX- LOOP-HELIX PROTEIN HEIR-1) - HOMO SAPIENS (HUMAN), 119 aa. [pcls:SWISSPROT-ID:Q02535 DNA-BINDING PROTEIN INHIBITOR ID-3 (ID-LIKE PROTEIN INHIBITOR HLH 1R21) (HELIX-LOOP-HELIX PROTEIN HEIR-1) - HOMO SAPIENS (HUMAN), 119 aa.	1.30E-60 (1)	1p36.13
247	cg43982507	3373	GATACCTTTGCGT g GGATCAAGCTTG[gap/CJTGTACTTGA CCGTTTTTATATA	gap	O	SILENT- NONCODI NG	eph	Human Gene SWISSPROT- ID: P98155 VERY LOW-DENSITY LIPOPROTEIN RECEPTOR PRECURSOR (VLDL RECEPTOR) - HOMO SAPIENS (HUMAN), 873 aa.	o	9 (9p24)
248	cg43982507	3739	CAAAAAATTTAT g AAACTAATTTTG[g ap/GJTACGTATGA ATGATATCTTTGA CCT	gap	O	SILENT- NONCODI NG	ebh	Human Gene SWISSPROT- ID:P98155 VERY LOW-DENSITY LIPOPROTEIN RECEPTOR PRECURSOR (VLDL RECEPTOR) - HOMO SAPIENS (HUMAN), 873 aa.	<u>о</u>	9 (9p24)
249	cg43982507	514	CCTCCTTCTCCCC A CTTTCCCCTCCC[ACJGCCCCCACCT TCTTCCTCCTTTC GG		O	SILENT- NONCODI NG	ebh	Human Gene SWISSPROT- ID:P98155 VERY LOW-DENSITY LIPOPROTEIN RECEPTOR PRECURSOR (VLDL RECEPTOR) - HOMO SAPIENS (HUMAN), 873 aa.	0	9 (9p24)

(11q23)	11 (11q23)	ო
1.80E-203 11	1.80E-203	0
Human Gene SWISSNEW- ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa. pcls:SWISSPROT-ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa.	Human Gene SWISSNEW- ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa. pcis:SWISSPROT-ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa.	Human Gene SWISSPROT- ID:P51178 1- PHOSPHATIDYLINOSITOL-4,5- BISPHOSPHATE PHOSPHODIESTERASE DELTA 1 (EC 3.1.4.11) (PLC-DELTA-1) (PHOSPHOLIPASE C-DELTA-1) (PLC-III) - HOMO SAPIENS (HUMAN), 756 aa.
ebh	hde	esterase
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
_ de D	Т	<u>ن</u>
CTGCCCTGCCAC (CTGTCTGTCTGTA) [gap/T]CCAAAGAA GTTCTGGTATGAA CTTG	CTGCCCTGCCAC (CTGTCTGTCTGTCTGTCTGTCTGTGCAAGAAGTTCTGGTATGAACTTG	TCCCTCCAGGACT AGGCTGGAGGAA[G/C]CCAGTGGGG TCCCCCTGAGT GGGC
ł	1371	2376
cg41554010 1371	cg41554010	cg43984905
250	251	252

r.	2	11 (11pter)
0	0	1.80E-195
Human Gene SWISSPROT- ID:P51178 1- PHOSPHATIDYLINOSITOL-4,5- BISPHOSPHATE PHOSPHODIESTERASE DELTA 1 (EC 3.1.4.11) (PLC-DELTA-1) (PHOSPHOLIPASE C-DELTA-1) (PLC-III) - HOMO SAPIENS (HUMAN), 756 aa.	glycoprotein Human Gene SWISSPROT-ID:P08183 MULTIDRUG RESISTANCE PROTEIN 1 (P-GLYCOPROTEIN 1) - HOMO SAPIENS (HUMAN), 1280 aa.	glycoprotein Human Gene SWISSPROT- ID:P16070 CD44 ANTIGEN PRECURSOR (PHAGOCYTIC GLYCOPROTEIN I) (PGP-1) (HUTCH-I) (EXTRACELLULAR MATRIX RECEPTOR-III) (ECMR-III) (GP90 LYMPHOCYTE HOMING/ADHESION RECEPTOR) (HERMES ANTIGEN) (HEPARAN SULFATE PROTEOGLYCAN) (EPICAN) (CDW44) - HOMO SAPIENS (HUMAN), 742 aa.
esterase	glycoprotein	glycoprotein
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
O	∢	<
O	ပ	ပ
CACATGTGGGGA CAGGGCTGGTGT G[G/C]CTGCTCCC AGCCTCTTGCTCA GAGC	CTAAAGTCGGAGT ATCTTCCAA[G AATTTCACGTCT TGCCGCCGTTC CA	TTTCTAGAGGGG GTCTGTTGAAGAT IG/AJTGTAACTAGT ACACCCCAACCC CCA
	382	267
cg43984905 2440	cg43992911	cg43932434
253	254	255

(11pter)	1 (1921)
1.80E-195	3.10E-185
glycoprotein Human Gene SWISSPROT- ID:P16070 CD44 ANTIGEN PRECURSOR (PHAGOCYTIC GLYCOPROTEIN I) (PGP-1) (HUTCH-I) (EXTRACELLULAR MATRIX RECEPTOR-III) (ECMR-III) (GP90 LYMPHOCYTE HOMING/ADHESION RECEPTOR) (HERMES ANTIGEN) (HYALURONATE RECEPTOR) (HEPARAN SULFATE PROTEOGLYCAN) (EPICAN) (CDW44) - HOMO SAPIENS (HUMAN), 742 aa.	glycoprotein Human Gene SWISSNEW- ID:P15813 T-CELL SURFACE GLYCOPROTEIN CD1D PRECURSOR (CD1D ANTIGEN) (R3G1) - HOMO SAPIENS (HUMAN), 335 aa.lpcis:SWISSPROT-ID:P15813 T-CELL SURFACE GLYCOPROTEIN CD1D PRECURSOR (CD1D ANTIGEN) (R3G1) - HOMO SAPIENS (HUMAN), 335 aa.
SILENT- NONCODI NG	SILENT- NONCODI NG
O	O
CCCCAACCCCCA A ACTCAGTGGAAA [A/G]CAATGCCCA GGGATTAGGCTAT GGA	GCGCAGGTCAGA A GGGCGGCCGCAG CAAGGCCTCCG CGAGGTCCCCAC GCCGG
306	366
cg43932434 306	cg43318219
256	257

7	2	6 (6p25)	6 (6p25)
8.20E-67	8.20E-67	8.90E-61	8.90E-61
glycoprotein Human Gene Similar to SWISSPROT-ID:Q08878 FIBULIN-1, ISOFORM C PRECURSOR (BASEMENT-MEMBRANE PROTEIN 90) (BM-90) - MUS MUSCULUS (MOUSE), 685 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:Q08878 FIBULIN-1, ISOFORM C PRECURSOR (BASEMENT-MEMBRANE PROTEIN 90) (BM-90) - MUS MUSCULUS (MOUSE), 685 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P49222 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - MUS MUSCULUS (MOUSE), 690 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P49222 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - MUS MUSCULUS (MOUSE), 690 aa.
glycoprotein	glycoprotein	glycoprotein	glycoprotein
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
dap	deß	 	F
_	—	U	⋖
CTCTATACTGTAC / ACTCACCCATAAIT /gapjTCAAACAATT ACACCATGGTATA AA	TCTATACTGTACA CTCACCCATAATIT /gapJCAAACAATTA CACCATGGTATAA AG	GCCGAATAGCCT GGGTTTGGAAAA G[C/T]ATGTTTTG AAATATGTGGGAT CTC	TACTGACCTAAAT CACACCCTAGAC[A/TITATCAGAGGG AAATTCTGACCAT AA
1954	1955	1411	385
cg43967861	cg43967861	cg43965366	cg43965366
258	259	260	261

12	7		-	
3.30E-54	1.20E-224	1.20E-224	1.20E-224	1.60E-206
glycoprotein Human Gene Similar to SWISSPROT-ID:P13983 EXTENSIN PRECURSOR (CELL WALL HYDROXYPROLINE-RICH GLYCOPROTEIN) - NICOTIANA TABACUM (COMMON TOBACCO), 620 aa.	Human Gene SWISSPROT- ID:P50219 HOMEOBOX PROTEIN HB9 - HOMO SAPIENS (HUMAN), 401 aa.	Human Gene SWISSPROT- ID:P50219 HOMEOBOX PROTEIN HB9 - HOMO SAPIENS (HUMAN), 401 aa.	Human Gene SWISSPROT- ID:P50219 HOMEOBOX PROTEIN HB9 - HOMO SAPIENS (HUMAN), 401 aa.	Human Gene TREMBLNEW-ID:G2896172 LIM HOMEOBOX PROTEIN COFACTOR - HOMO SAPIENS (HUMAN), 373 aa.
glycoprotein	нотеорох	homeobox	homeobox	homeobox
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
<u>o</u>	ပ	O	<u> </u>	U
∢	gap	gap	O	-
TGTCCTTGAAGAA A CATGCACTTGGC[A/G]CGGATGGCA CAAGCAAAATGGT AGA	CCCGCGCCCCAG TAGGAGCCCCGC Glgap/GlCCCAGCA GGTGCGGCGCGC	CCAGCAGGTGCG GCGCGCACGGAG C[gap/G]CGCCGG CCGGCGCTTCT CCGGGAG	TGAAACTTGAAAC CGCCTCTGGAGC[C/TJGCCATTCTGC AGAGTATTTGGAA AA	TCCAAGAAAGGGT CATGGAAGCTTAI T/CJTGGGAATAAT CCTCTCAATTAGA AA
1255	1397	1423	1817	939
cg43322513 1255	cg41637704	cg41637704	cg41637704	cg43980506
262	263	264	265	266

10	16 (16q22)	16 (16q22)	7 (7p21)
1.30E-156 10	2.00E-220	2.00E-220	3.40E-108
Human Gene SWISSPROT- ID:P37980 INORGANIC PYROPHOSPHATASE (EC 3.6.1.1) (PYROPHOSPHATE PHOSPHO- HYDROLASE) (PPASE) - BOS TAURUS (BOVINE), 289 aa.	Human Gene SPTREMBL- ID:Q13194 11-BETA- HYDROXYSTEROID DEHYDROGENASE TYPE 2 - HOMO SAPIENS (HUMAN), 405 aa.	Human Gene SPTREMBL-ID:Q13194 11-BETA-HYDROXYSTEROID DEHYDROGENASE TYPE 2 -HOMO SAPIENS (HUMAN), 405 aa.	Human Gene Homologous to SWISSPROT-ID:P05231 INTERLEUKIN-6 PRECURSOR (IL- 6) (B-CELL STIMULATORY FACTOR 2) (BSF-2) (INTERFERON BETA-2) (HYBRIDOMA GROWTH FACTOR) - HOMO SAPIENS (HUMAN), 212 aa.
hydrolase	hydroxyster oid	hydroxyster oid	interleukin
SILENT- NONCODI NG	SILENT- hyd NONCODI oid NG	SILENT- hyd NONCODI oid NG	SILENT- NONCODI NG
<u> </u>	gap	gap	—
<u>ග</u>	တ	O	gap
GGGGGGTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT	CTGGGGGTTTTC GGGGAGGAACCA A[G/gap]GGCTCAC GGAGCCTCCTGT GCTGCA	GGGGGTTTTCGG (GGAGGAACCAAG G[G/gap]CTCACGGAGCTCCTGTGCT GCAGT	GAGTTAATTTATG TAAGTCATATTT[g ap/TJATATTTTTAA GAAGTACCACTTG AA
100	503	505	1031
cg43961305 100	cg43998672	cg43998672	cg42908571
267	268	269	270

7 (7p21)	2 (2q35)	ഹ
3.40E-108 7 (7p21)	9.60E-191 2 (2q35)	1.60E-156
Human Gene Homologous to SWISSPROT-ID:P05231 INTERLEUKIN-6 PRECURSOR (IL- 6) (B-CELL STIMULATORY FACTOR 2) (BSF-2) (INTERFERON BETA-2) (HYBRIDOMA GROWTH FACTOR) - HOMO SAPIENS (HUMAN), 212 aa.	interleukinre Human Gene SWISSPROT- cept ID:P25025 HIGH AFFINITY INTERLEUKIN-8 RECEPTOR B (IL- 8R B) (CXCR-2) (GRO/MGSA RECEPTOR) (IL-8 RECEPTOR TYPE 2) - HOMO SAPIENS (HUMAN), 360 aa.	Human Gene SWISSPROT- ID:P46926 PUTATIVE GLUCOSAMINE-6-PHOSPHATE ISOMERASE (EC 5.3.1.10) (GLUCOSAMINE- 6-PHOSPHATE DEAMINASE) (OSCILLIN) (KIAA0060) - HOMO SAPIENS (HUMAN), 289 aa.
interleukin	interleukinre cept	isomerase
SILENT- NONCODI NG	SILENT- inter NONCODI cept NG	SILENT- NONCODI NG
I	U	O
de B	L-	∢
CTTACCTCAAATA (SAATGCTTIGGCTAACTTIGGCTAACTTIGGCTAACTTTTTTAAAGAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAAATATTTAAAGAAAATATTTAAAGAAATATTTAAAGAAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAAATATTTAAAGAAAATATTTAAAGAAATATTTAAAGAAATATTTAAAGAAAATATTTAAAGAAATATTTAAAGAAAATATTTAAAGAAAATATTAAAGAAAATATTAAAGAAAATATTAAAGAAAATATTAAAAGAAAATATTAAAAGAAAATATTAAAAGAAAAATAAT	CAGCCCCCATTGT GGTCACAGGAAG[T/C]AGAGGAGGC CACGTTCTTACTA GTT	CCCAACCTGGGTT. TGGCAGACATCA[A/GJAATGATGGAG TACATTTTGCAGA TA
1178		1133
cg42908571 1178	cg42164914 1617	cg43958501
271	272	273

	10	X (Xq21.3)
1.60E-156 5	0	0
Human Gene SWISSPROT- ID:P46926 PUTATIVE GLUCOSAMINE-6-PHOSPHATE ISOMERASE (EC 5.3.1.10) (GLUCOSAMINE- 6-PHOSPHATE DEAMINASE) (OSCILLIN) (KIAA0060) - HOMO SAPIENS (HUMAN), 289 aa.	Human Gene SWISSPROT- ID:Q04759 PROTEIN KINASE C, THETA TYPE (EC 2.7.1) (NPKC- THETA) - HOMO SAPIENS (HUMAN), 706 aa.	Human Gene SWISSPROT- ID:Q06187 TYROSINE-PROTEIN KINASE BTK (EC 2.7.1.112) (BRUTON'S TYROSINE KINASE) (AGAMMAGLOBULINAEMIA TYROSINE KINASE) (ATK) (B CELL PROGENITOR KINASE) (BPK) - HOMO SAPIENS (HUMAN), 659 aa.
isomerase	kinase	kinase
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
V O	<u>0</u>	Ο
CACCCCAGGTT CTCCTAGTTCAGA [G/A]AAAAGCTGT GAAAGTGGAAGA AGGA	TTTATTCTATTCCT ATCTGTGGATG[T/ GJGTAAATGGCTG GGGGCCAGCCC	AGCCTTTGTGCTC A CCACTCAATACA[A CCJAAAGGCCCCTC TCTACATCTGGGA A
805	2710	2259
cg43958501	cg43090990	cg42879455
274	275	276

0 X (Xq21.3)	1,40E-290 9	1.40E-290 9	1.40E-290 9
Human Gene SWISSPROT- ID:Q06187 TYROSINE-PROTEIN KINASE BTK (EC 2.7.1.112) (BRUTON'S TYROSINE KINASE) (AGAMMAGLOBULINAEMIA TYROSINE KINASE) (ATK) (B CELL PROGENITOR KINASE) (BPK) - HOMO SAPIENS (HUMAN), 659 aa.	Human Gene SPTREMBL- ID:Q92749 TYPE I PHOSPHATIDYLINOSITOL-4- PHOSPHATE 5-KINASE BETA (EC 2.7.1.68) (STM-7 PROTEIN) - HOMO SAPIENS (HUMAN), 540 aa.	Human Gene SPTREMBL- ID:Q92749 TYPE I PHOSPHATIDYLINOSITOL-4- PHOSPHATE 5-KINASE BETA (EC 2.7.1.68) (STM-7 PROTEIN) - HOMO SAPIENS (HUMAN), 540 aa.	Human Gene SPTREMBL- ID:Q92749 TYPE I PHOSPHATIDYLINOSITOL-4-
kinase	kinase	kinase	kinase
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
O	F	∢	 -
	O	O	gap
AAAAAGGCCCCTC A TCTACATCTGGG[A/GJATGCACCTCT TCTTTGATTCCCT GG	AGCAACTTGGCTG AGCCCCACTACA[C/TJACAGAGAAAT CATCAACCTGACT TA	TAAGAGTTTTCAA GATGTCAAACTT[C /AJAGGCTGATCAG CAGATGGGATGT GA	TTTTTAAAAATCCA gap TCCACACACATIga p/TJGGTAAATTAA
2283	2151	2200	2451
cg42879455	cg43971741	cg43971741	cg43971741 2451
277	278	279	280

O	o	ဖွ	_	
		7.80E-173 16	-79 1	- 55
5.60E	5.60E-267	7.80E		5.30E-55
Human Gene SWISSPROT-ID:P49840 GLYCOGEN SYNTHASE KINASE-3 ALPHA (EC 2.7.1.37) (GSK-3 ALPHA) - HOMO SAPIENS (HUMAN), 483 aa.	Human Gene SWISSPROT- ID:P49840 GLYCOGEN SYNTHASE KINASE-3 ALPHA (EC 2.7.1.37) (GSK-3 ALPHA) - HOMO SAPIENS (HUMAN), 483 aa.	Human Gene SPTREMBL- ID:Q15599 TYROSINE KINASE ACTIVATOR PROTEIN 1 (TKA-1) - HOMO SAPIENS (HUMAN), 450 aa.	Human Gene Similar to SPTREMBL-ID:Q15599 TYROSINE KINASE ACTIVATOR PROTEIN 1 (TKA-1) - HOMO SAPIENS (HUMAN), 450 aa.	Human Gene Similar to SWISSPROT-ID:P20505 30 KD PROTEIN KINASE HOMOLOG (EC 2.7.1) (PROTEIN B1) - VACCINIA VIRUS (STRAIN COPENHAGEN), 300 aa.
kinase	kinase	kinase	kinase	kinase
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
gap	gap	O	ပ	∢
O	O	gap	<	O
AACGTCGATTCGC G ACCGTCCAACCT[G/gap]GCCCCGCC CCTCCTACAGCTG TAAC	ACGTCGATTCGCA CCGTCCAACCTG[G/gap]CCCCGCCCCCCCCAACTGTAACTACAGCTGTAACTACAGCTGT	1		GGAAAGG SACACTG[ATTATCAC TGATCAGG
1996	1997	1535	306	1876
cg43947749 1996	cg43947749	cg44131752	cg43917718	cg43928048
281	282	283	284	285

9 (9p21)	19 (19q13.1)
2.60E-53	0
kinaseinhibit Human Gene Similar to SWISSPROT-ID:P42771 CYCLIN- DEPENDENT KINASE 4 INHIBITOR A (CDK4I) (P16-INK4) (P16-INK4A) (MULTIPLE TUMOR SUPPRESSOR 1) (MTS1) - HOMO SAPIENS (HUMAN), 156 aa.	kinaserecep Human Gene SWISSNEW- tor KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.lpcls:SWISSPROT-ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.
SILENT- kina NONCODI or NG	SILENT- kina NONCODI tor NG
	,
Σ	O
CCCTCCGGATTC CGGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGCGC	TCCAAGCTAAGCA A CTGCCACTGGGG[AGJAAACTCCACCTTCCCACTTCCCACTTCCCACCTTCCCACCTACCACC
208	2943
cg42714751 208	cg43322545 2943
286	287

288	cg43322545 3037	3037	CCACCTCCATCCC C AGACAGGTCCCT[C/G]CCCTTCTCTG TGCAGTAGCATCA CC	<u>ග</u>	SILENT- Kin NONCODI for NG	aserecep	kinaserecep Human Gene SWISSNEW- ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa. pcls:SWISSPROT-ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.	F 5 0	19 (19q13.1)
289	cg43322545	3038	CACCTCCATCCCA C GACAGGTCCCTC[C/G CCTTCTCTGT GCAGTAGCATCAC CT	0	SILENT- kin NONCODI tor NG	kinaserecep	kinaserecep Human Gene SWISSNEW- tor ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa. [pcls:SWISSPROT-ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.		19 (19q13.1
290	cg43980494	1040	GTCTGATAGAAGA A GGAGCAGGAGAA[A/G]CAAATCGTTA AAACCTAGCGAAT TC	9	SILENT- NONCODI NG	kinesin	Human Gene SPTREMBL- ID:Q14807 KID (KINESIN-LIKE DNA BINDING PROTEIN) - HOMO SAPIENS (HUMAN), 665 aa.		16

			_	
7.90E-79	7.90E-79	7.90E-79	2.30E-71	0
	Human Gene Similar to SPTREMBL- ID:P91197 SIMILAR TO LIGAND- GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.	Human Gene Similar to SPTREMBL- ID:P91197 SIMILAR TO LIGAND- GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.	REMBL- AND- ROTEIN ANS,	Human Gene SWISSPROT- ID:P15498 VAV PROTO- ONCOGENE - HOMO SAPIENS (HUMAN), 846 aa.
misc_chann el	misc_chann el	misc_chann el	misc_chann el	oncogene
SILENT- mi NONCODI el NG	SILENT- NONCODI el NG	SILENT- NONCODI el NG	SILENT- m NONCODI el NG	SILENT- NONCODI NG
O	O	O	O	gap
CGAGCGGCACCC TAGAGCCTGCACC CIT/GICCTCACC GTCGTCACC GTCCTCACC GTCCTTCTGCGTC CCCC	AGGAGCCCTCTTC T GGTGTCCCGAG[T/C]GCCACGGTCA AGACCCGCAGCA CCA	CGGTCAAGACCC A GCAGCACCAAAG C[A/G]CCGCCCC GCACCTGCCCCT	GAGCCGTGTGGC A TGTGGCCTCCGG G[A/C]GGCGGTGG ACGCGTGCGCT TCATC	GGGTGCACGGCC g GGCCCTGGGCAG G[gap/C]GTAGCCA TGGAGCTGTGGC GCCAAT
1440	1860	1890	1541	68
cg21413267	cg21413267	cg21413267	cg42481172	cg39518465
296	297	298	299	300

1.40E-84	NONCODI NG NG	Company Comp	ARGBP2A - HOMO SAPIENS INCOMBAN GENE Similar to TREMBLNEW-ID:62952331 ARGABL-INTERACTING PROTEIN ARGBP2A - HOMO SAPIENS (HUMAN), 666 aa.	Company Comp
0000				
ICII ENT.	NG	SILENT- NONCOD NG	SILENT- NONCOD NG	SILENT- NONCOD NG
·)	-	O	
Ī				
	ATGGGGCCGGTG 19 TCTCGCCAGGAG G[gap/C]GCAGAGC CGGCTCCAGGGC CAGCGC	AGCATTTGAGGAA C GCATAACTGACG C/TJGTGAAGGGG GTGTGGGGTACTT GCC	AGCATCTGCAGAC A GACCCCGCAGC[A/CJTTCCCTCGG ACCCCCTCGAA GCC	GCTGTGCA CAGGGA[AT] CCAGGCAGA CCCAGCAAA
	927	235	2295	22
	cg41972699 627	cg40333812	cg43280482	cg44014837
	양	18	10	10

3 (3q26.3)	-	2	-
0	4.60E-246	2.60E-227	1.90E-202
Human Gene SWISSPROT- ID:P07202 THYROID PEROXIDASE PRECURSOR (EC 1.11.1.8) (TPO) - HOMO SAPIENS (HUMAN), 933 aa.		Human Gene SWISSPROT- ID:Q14642 TYPE I INOSITOL-1,4,5- TRISPHOSPHATE 5- PHOSPHATASE (EC 3.1.3.56) (5PTASE) - HOMO SAPIENS (HUMAN), 412 aa. pcls:SPTREMBL- ID:Q14642 INOSITOL 1,4,5- TRIPHOPHATE 5-PHOSPHATASE - HOMO SAPIENS (HUMAN), 412 aa.	Human Gene SWISSPROT- ID:P36876 PROTEIN PHOSPHATASE PP2A, 55 KD REGULATORY SUBUNIT, ALPHA ISOFORM (PROTEIN PHOSPHATASE PP2A B SUBUNIT ALPHA ISOFORM) (ALPHA-PR55) - RATTUS NORVEGICUS (RAT), 447 aa.
peroxidase	phosphatas e	phosphatas e	phosphatas e
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
gap	Ø	<u>ග</u>	O
A	—	∢	O
CAGCACAGCGAG CGCTCTCATTCTG [A/gap]CCTTTTTC CTCTTCTCAGCCA	TCTGTAGAGCTCT GAAAAGGTTGACI T/GJATATAGAGGT CTTGTATGTTTTTA	GACAGACGAGAC AGTGAGGTATGTG [A/G]GGCTGCTCC GGAATGGTCCGG AGGC	TAACTATGCAAGA CAAGACTTGGTC C/GJTCACGTTCGC GTCTCTAGTTGAT TT
3178	2958	1537	581
cg41626506 3178	cg43918944	cg43988365	cg43969460
305	306	307	308

2 (2p23)	O	1 (1p21)
1.60E-181 2 (2p23)	1.20E-89	5.40E-284
phosphatas Human Gene SWISSPROT- ID:P37140 SERINE/THREONINE PROTEIN PHOSPHATASE PP1- BETA CATALYTIC SUBUNIT (EC 3.1.3.16) (PP-1B) - HOMO SAPIENS (HUMAN), RATTUS NORVEGICUS (RAT), MUS MUSCULUS (MOUSE),,	phosphatas Human Gene Similar to swissprot-iD:P39687 POTENT HEAT-STABLE PROTEIN HEAT-STABLE PROTEIN PHOSPHATASE 2A INHIBITOR 11PP2A (HLA-DR ASSOCIATED PROTEIN I) (PHAPI) (ACIDIC NUCLEAR PHOSPHOPROTEIN PP32) (CEREBELLAR LEUCINE RICH ACIDIC NUCLEAR PROTEIN) - HOMO SAPIENS (HUMAN), 249 aa.	Human Gene SWISSPROT- ID:P22001 VOLTAGE-GATED POTASSIUM CHANNEL PROTEIN KV1.3 (HPCN3) (HGK5) (HUKIII) (HLK3) - HOMO SAPIENS (HUMAN), 523 aa.
phosphatas e	phosphatas einhib	potassium_ channel
SILENT- NONCODI NG	SILENT- phosp NONCODI einhib NG	SILENT- potassir NONCODI channel NG
O	<u>F-</u>	<u> </u>
 -	O	ග
AATTAAAACTCTA GGTGTATACTTA[T /CJATGGAACTAGT TTATTTCCTATTTA	TGCTCGCGCCGT GCCACTAAGGTCA [C/T]TCCCGCCTC CGAGAGCCCAGA GCCG	CTTTTCCCTCTTA CCCTCTCTCT[G/TAACATCGTAA ACAACAGACTTAC GT
	215	
cg43933809 362	cg43931444	cg42937321 1977
309	310	311

SILENT- potassium_ Human Gene SWISSPROT- 5.40E-284 1 (1p21) NONCODI channel ID:P22001 VOLTAGE-GATED NG RV1.3 (HPCN3) (HGK5) (HUMII) (HLK3) - HOMO SAPIENS (HUMAN), 523 aa.	SILENT- potassium_ Human Gene SWISSPROT- 1.80E-205 11 NONCODI channel ID:P48048 ATP-SENSITIVE NG CHANNEL 1 (POTASSIUM CHANNEL, INWARDLY J, RECTIFYING, SUBFAMILY J, MEMBER 1) (ATP-REGULATED POTASSIUM CHANNEL ROM-K) (KIR1.1) - HOMO SAPIENS (HUMAN), 391 aa.
cg42937321 1983 CCTCTTACCCTCT C T CTCTCTGAACAT[C // IGTAAACAACAG ACTTACGTTAAAC	CAAAATGTAACAG A G TGGCTTTTCAAC[A /G]GGAGTAAAGCA AAGTCTCTAAAGC
2937321 1983 (cg40991963 1357 (
312 cg4	313 cg4

(1q25.2)
0
prostaglandi Human Gene SWISSNEW- ID:P35354 PROSTAGLANDIN G/H SYNTHASE 2 PRECURSOR (EC 1.14.99.1) (CYCLOOXYGENASE -2) (COX-2) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE 2) (PROSTAGLANDIN H2 SYNTHASE 2) (PGH SYNTHASE 2) (PHS II) - HOMO SAPIENS (HUMAN), 604 aa.lpcls:SPTREMBL- ID:Q16876 PROSTAGLANDIN ENDOPEROXIDE SYNTHASE-2 PRECURSOR (EC 1.14.99.1) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE) (PROSTAGLANDIN SYNTHASE) (PROSTAGLANDIN SYNTHASE) (PROSTAGLANDIN SYNTHASE) (PUMAN), 604 aa.
SILENT- NONCODI NG
A
ပ
AAAGATGTTTGAA G TACTTAAACACT[G AJTCACAAGATGG CAAAATGCTGAAA G
2332
cg43951366 2332
814 4

1 (1q25.2)	1 (1p31.2)
0	1.40E-211
prostaglandi Human Gene SWISSNEW- ID:P35354 PROSTAGLANDIN G/H SYNTHASE 2 PRECURSOR (EC 1.14.99.1) (CYCLOOXYGENASE -2) (COX-2) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE 2) (PROSTAGLANDIN H2 SYNTHASE 2) (PGH SYNTHASE 2) (PHS II) - HOMO SAPIENS (HUMAN), 604 aa.lpcls:SPTREMBL- ID:Q16876 PROSTAGLANDIN ENDOPEROXIDE SYNTHASE) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE) (PROSTAGLANDIN- ENDOPEROXIDE SYNTHASE) (PROSTAGLANDIN SYNTHASE) (PROSTAGLANDIN SYNTHASE) (PROSTAGLANDIN SYNTHASE) (PROSTAGLANDIN SYNTHASE) (HUMAN), 604 aa.	prostaglandi Human Gene SPTREMBL-ID:000325 PROSTAGLANDIN EP3 RECEPTOR SUBTYPE ISOFORM - HOMO SAPIENS (HUMAN), 402 aa.
prostaglandi n	prostaglandi n
SILENT- NG NG	SILENT- NONCODI NG
O	O
TGGTGGAGCCAC TGCAGTGTTATCT[TCJAAAATAAGAA TATTTGTTGAGA TA	CACTTAACTTGCA TGTGCACAGCTT[T/CJTGGTAACAAA TATCGCTAAACCT TA
	1431
cg43951366 2829	cg43306254
315	316

1 (1p31.2)	11 (11q21)	2 (2q13)
1.40E-211 1	2.40E-146	2.40E-82
prostaglandi Human Gene SPTREMBL- ID:000325 PROSTAGLANDIN EP3 RECEPTOR SUBTYPE ISOFORM - HOMO SAPIENS (HUMAN), 402 aa.	Human Gene Homologous to SWISSNEW-ID:P09237 MATRILYSIN PRECURSOR (EC 3.4.24.23) (PUMP-1 PROTEASE) (UTERINE METALLOPROTEINASE) (MATRIX METALLOPROTEINASE- 7) (MMP-7) (MATRIN) - HOMO SAPIENS (HUMAN), 267 aa. pcls:SWISSPROT-ID:P09237 MATRILYSIN PRECURSOR (EC 3.4.24.23) (PUMP-1 PROTEASE) (UTERINE METALLOPROTEINASE- 7) (MMP-7) (MATRIN) - HOMO SAPIENS (HUMAN), 267 aa.	Human Gene Similar to SWISSPROT-ID:P25155 COAGULATION FACTOR X PRECURSOR (EC 3.4.21.6) (STUART FACTOR) (VIRUS ACTIVATING PROTEASE) (VAP) - GALLUS GALLUS (CHICKEN), 475 aa.
prostaglandi n	protease	protease
SILENT- principal number of number o	SILENT- NONCODI NG	SILENT- NONCODI NG
H	<u> -</u>	O
K	O	O
ATGTGATTAATTA TGTGATGAAAAC[A/I]TTTTTATAAA TGATCTTGGTCTA T	CAATCAGAATTGA TAAGCACTGTTC[C/IJTCCACTCCAT TTAGCAATTATGT CA	TCCATCCCTCTTT TGGGCTCTTCTG[G/CJAGGGAAGTAA CATTTACTGAGCA CC
	1064	1703
cg43306254 1666	cg42918089	cg44032168
317	318 8	310

(11922)	6 (6pter)	6 (6pter)
2.40E-59 11 (1-1)	1.60E-124 6 (6pter)	1.60E-124 6 (6pter)
Human Gene Similar to SWISSPROT-ID:P50280 MATRILYSIN PRECURSOR (EC 3.4.24.23) (PUMP-1 PROTEASE) (UTERINE METALLOPROTEINASE) (MATRIX METALLOPROTEINASE- 7) (MMP-7) (MATRIN) - RATTUS NORVEGICUS (RAT), 267 aa.	Human Gene Homologous to SWISSPROT-ID:P16083 NAD(P)H DEHYDROGENASE (QUINONE) 2 (EC 1.6.99.2) (QUINONE REDUCTASE) (DT-DIAPHORASE) (AZOREDUCTASE) (PHYLLOQUINONE REDUCTASE) (MENADIONE REDUCTASE) HOMO SAPIENS (HUMAN), 231 aa.	Human Gene Homologous to SWISSPROT-ID:P16083 NAD(P)H DEHYDROGENASE (QUINONE) 2 (EC 1.6.99.2) (QUINONE REDUCTASE) (DT-DIAPHORASE) (AZOREDUCTASE) (PHYLLOQUINONE REDUCTASE) (MENADIONE REDUCTASE) - HOMO SAPIENS (HUMAN), 231 aa.
protease	reductase	reductase
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
O	O	O
 	∢	gap
TACCCGGAAGTTG AGCTCAATTTCATT /CJTTCTGTTTTCT GGCCACAACTGC CA	CCCAGTCCTGCG GCTCCTACTGGG G[A/C]GTGCGCTG GTGGAAGATTG CTGGA	TACTGGGGAGTG CGCTGGTCGGAA G[gap/G]ATTGCTG GACTCGCTGAAG AGAGAC
	175	191
cg43154190 1250	cg43927549	cg43927549
320	321	322

6 (6pter)	0	က	-
1.60E-124 6 (6pter)	3.30E-207	1.70E-200	2.10E-124
Human Gene Homologous to SWISSPROT-ID:P16083 NAD(P)H DEHYDROGENASE (QUINONE) 2 (EC 1.6.99.2) (QUINONE REDUCTASE) (DT-DIAPHORASE) (AZOREDUCTASE) (PHYLLOQUINONE REDUCTASE) (MENADIONE REDUCTASE) - HOMO SAPIENS (HUMAN), 231 aa.	Human Gene SWISSPROT- ID:O15142 ACTIN-LIKE PROTEIN 2 - HOMO SAPIENS (HUMAN), 394 aa.	Human Gene SWISSPROT- ID:Q14012 CALCIUM/CALMODULIN- DEPENDENT PROTEIN KINASE TYPE I (EC 2.7.1.123) (CAM KINASE I) - HOMO SAPIENS (HUMAN), 370 aa.	Human Gene Homologous to SPTREMBL-ID:000379 DELTA- CATENIN - HOMO SAPIENS (HUMAN), 792 aa.
reductase	struct	struct	struct
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
O	O	da O	O
gap	A	U	4
CGGTCCGTGGTC gap CCCGGGGGCGCA G[gap/G]TCGCAGC GCTCCCGCCCTC CAGGCG	TTCTCAAAAGGCT GGGGGTATTTAT[A/GJTAAGAACTTA TTCCAAAGTGACT CT	AGGAAAGCCGGA GAATTGGGGCAC G[C/gap]AAGAGGG GGGGCTTTGATG ACCCGC	AGATTCATCAGAA TAGGATTTTTGC[A /CJAAATCCCACCC ATATGCTGTTGAG C
52	780	113	1926
cg43927549 (cg43947066	cg43923264	cg43942332
323	324	325	326

72	7 (7 q32)	17
4.80E-110 12	3.50E-74	1.20E-55
Human Gene Homologous to SPTREMBL-ID:Q28910 MUCIN - BOS TAURUS (BOVINE), 600 aa (fragment).	Human Gene Similar to SWISSNEW- ID:P12273 PROLACTIN-INDUCIBLE PROTEIN PRECURSOR (SECRETORY ACTIN-BINDING PROTEIN) (SABP) (GROSS CYSTIC DISEASE FLUID PROTEIN 15) (GCDFP-15) (GP17) - HOMO SAPIENS (HUMAN), 146 aa. pcls:SWISSPROT-ID:P12273 PROLACTIN-INDUCIBLE PROTEIN PRECURSOR (SECRETORY ACTIN-BINDING PROTEIN) (SABP) (GROSS CYSTIC DISEASE FLUID PROTEIN 15) (GCDFP-15) - HOMO SAPIENS (HUMAN), 146 aa.	Human Gene Similar to SWISSPROT-ID:P19065 SYNAPTOBREVIN 2 (VESICLE ASSOCIATED MEMBRANE PROTEIN 2) (VAMP-2) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 115 aa.
struct	struct	struct
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
—	<u> </u>	<u> </u>
ပ	O	4
CCGCTGTCTCTGT G CTTCGCTTTTTA[G //IJCAAGAAGAAT AATGCGACGAAAA	CCACTTCTCTGGG ACACATTGCCTT[C //IJTGTTTTCTCCA GCATGCGCTTGCT C	CATCATCATCATA GITTACTTCAGCIA MICTTAAATCCCC GAGGAGTCTGCC CT
580	946	546
cg43274705 580	cg42207316	cg43927885
327	328	329

24.2		
12 (12q24.2)	∞	œ
Q	9.80E-269	9.20E-83
Human Gene SWISSPROT- ID:P29475 NITRIC-OXIDE SYNTHASE, BRAIN (EC 1.14.13.39) (NOS, TYPE I) (NEURONAL NOS) (NNOS) - HOMO SAPIENS (HUMAN), 1434 aa.	Human Gene SWISSPROT-ID:P48651 PHOSPHATIDYLSERINE SYNTHASE I (SERINE-EXCHANGE ENZYME I) (EC 2.7.8) (KIAA0024) - HOMO SAPIENS (HUMAN), 473 aa.	Human Gene Similar to SPTREMBL- 9.20E-83 ID:Q42761 SQUALENE SYNTHASE (EC 2.5.1.21) (FARNESYL- DIPHOSPHATE FARNESYLTRANSFERASE) (FARNESYLTRANSFERASE) (PRESQUALENE-DI- DIPHOSPHOSPHATE SYNTHASE) - GLYCYRRHIZA GLABRA, 412 aa.
synthase	synthase	synthase
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
—	—	O
o O		
CTCTTGCCCAGCC gap GGCTGCAAGTTT[gap/TjGTAAGCGC GGGACAGACACT GCTGA	AGGTTACCAAACA C GGAATACAACAC[C/I]TCTCTCCCTT TTCTGCTCTAGAA GG	TGGGTGATGATCA T CTGTGCTGCTTG[1/CJGGCTCATGGC AGAGCATTCAGTG CC
5029	555	1565
cg40388639	cg43949316	cg43958714
330	331	332

1 (1923)	1 (1923)
3.20E-65 1 (1q23)	3.20E-65
Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa. pcls:SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.	Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa. Ipcls: SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.
synthase	synthase
SILENT- NONCODI NG	SILENT- NONCODI NG
ļ	U
O	F
ACAGACTGGCTG CAGCATTAGGAAT [C/TJAGGTCATTCC GAAACTCATCATT GA	GGTCATTCCGAAA CTCATCGAGT CJCAGGAAGAGA AGAGTTCAATCTT A
2508	2535
cg43275028 2508	cg43275028
333	334

1 (1923)	1 (1923)
3.20E-65	3.20E-65
Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa. pcis:SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.	Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa.lpcls:SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.
synthase	synthase
SILENT- NONCODI NG	SILENT- NONCODI NG
O	O
	7
AGAATGGCACTGA A ATTCGTTTCTC[A/G]AATTGTTGGTTCA	CTTTCACTTGGTG A CTGGAGAATTCA[A/GJAAGTCAAGAA CATGCTAAGCATA AG
2601	
cg43275028	cg43275028 2873
335	336

1 (1q23)	1 (1923)
3.20E-65	3.20E-65
Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa. pcls:SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.	Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa.lpds:SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.
synthase	synthase
SILENT- NONCODI NG	SILENT- NONCODI NG
O	O
	T.
TTCAAAAGTCAAG A AACATGCTAAGC[A/GJTAAGGGACCC AAGGTAGAAAGA GAT	TTCTCCTTCCAGA ATGAGGCCCTGG[A/G]AGGACCCTCCTGGTAGTGATCTGTTACTTAGTGATCTGTTACTTAGTTAG
2894	3073
cg43275028	cg43275028 3073
337	338

1 (1923)	4	17	1 (1p31.2)
3.20E-65	1.60E-236	2.00E-220	4.80E-212
Human Gene Similar to SWISSPROT-ID:P70490 MILK FAT GLOBULE-EGF FACTOR 8 PRECURSOR (MFG-E8) (O- ACETYL GD3 GANGLIOSIDE SYNTHASE) (AGS) (MFGM) - RATTUS NORVEGICUS (RAT), 427 aa. ipcls:SPTREMBL-ID:P70490 O- ACETYL GD3 GANGLIOSIDE SYNTHASE - RATTUS NORVEGICUS (RAT), 427 aa.	Human Gene SWISSPROT- ID:P25101 ENDOTHELIN-1 RECEPTOR PRECURSOR (ET-A) - HOMO SAPIENS (HUMAN), 427 aa.	Human Gene SWISSPROT- ID:P51575 P2X PURINOCEPTOR 1 (ATP RECEPTOR) (P2X1) (PURINERGIC RECEPTOR) - HOMO SAPIENS (HUMAN), 399 aa.	Human Gene SWISSPROT- ID:P43115 PROSTAGLANDIN E2 RECEPTOR, EP3 SUBTYPE (PROSTANOID EP3 RECEPTOR) (PGE RECEPTOR, EP3 SUBTYPE) - HOMO SAPIENS (HUMAN), 390 aa.
synthase	tm7	tm7	tm7
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
O	O	O	9
∢	ပ	O	H-
ACTACATAAGGAC A AGCAACATGCCT[A/GJTGGACATGAG AGAATTTGTCTTA CT	GAAAAAATCACA AGGCAACTGTGA[C/GJTCCGGGAATC TCTTCTCTGATCC	TCCGACCCCACA CACCCTGAGGGA G[C/G]CCTACCCT AGCCTCAGCCGC	ATAATCCATGCCT CTGAATATTAGA[T /GJTGGTTTCTTGG ATGGGATTTTGAA T
5590	1856	1684	1603
cg43275028 5590	cg43985000	cg39565524	cg43306266
339	340	341	342

1 (1p31.2)	1 (1p31.2)
4.80E-212	4.80E-212
Human Gene SWISSPROT- ID:P43115 PROSTAGLANDIN E2 RECEPTOR, EP3 SUBTYPE (PROSTANOID EP3 RECEPTOR) (PGE RECEPTOR, EP3 SUBTYPE) - HOMO SAPIENS (HUMAN), 390 aa.	Human Gene SWISSPROT- ID:P43115 PROSTAGLANDIN E2 RECEPTOR, EP3 SUBTYPE (PROSTANOID EP3 RECEPTOR) (PGE RECEPTOR, EP3 SUBTYPE) - HOMO SAPIENS (HUMAN), 390 aa.
tm7	1 tm7
SILENT- tm7 NONCODI NG	SILENT- NONCODI NG
O	O
gap	O
GGGATTTTGAATA gap TGCATTTAAGAA[g ap/C]GTTGGGAAG AATTTCACAGATG	GAATATGCATTTA G AGAAGTTGGGAA{ G/CJAATTTCACAG ATGATGATTGGAG GA
1641	1650
cg43306266 1641	cg43306266
343	344

L	×
8.20E-201 7	2.00E-197 X
Human Gene SWISSNEW- ID:Q99527 CHEMOKINE RECEPTOR-LIKE 2 (IL8-RELATED RECEPTOR DRY12) (FLOW- INDUCED ENDOTHELIAL G PROTEIN-COUPLED RECEPTOR GPR30) (GPCR-BR)- HOMO SAPIENS (HUMAN), 375 aa.[pds:SWISSPROT-ID:Q99527 CHEMOKINE RECEPTOR DRY12) (FLOW-INDUCED ENDOTHELIAL G PROTEIN-COUPLED RECEPTOR GPR30) - HOMO SAPIENS (HUMAN), 375 aa.[pcis:TREMBLNEW-ID:G2656121 G-PROTEIN COUPLED RECEPTOR - HOMO SAPIENS (HUMAN), 375	Human Gene SWISSPROT- ID:P50052 TYPE-2 ANGIOTENSIN II RECEPTOR (AT2) - HOMO SAPIENS (HUMAN), 363 aa.
tm7	tm7
SILENT- NG NG NG	SILENT- NONCODI NG
—	O
	gap
TCGGCAAATCTTG C AAAGCTGCAGGG[C/TJGCAGAGACAT GGATGTGACTTCC CA	AAGGCATAAGAAC gap TAGGAGCTGCTG[gap/GJACATTTCAA TATGAAGGGCAAC
683	439
cg43329467 683	cg2751286
345	346

		!	6.90E-109 3 (3q21)
3.20E-176 1	-173 1	1.10E-173 1	-109
	1.10E-173	1.10E	9.90E
Human Gene SWISSPROT- ID:P46089 PROBABLE G PROTEIN- COUPLED RECEPTOR GPR3 (ACCA ORPHAN RECEPTOR) - HOMO SAPIENS (HUMAN), 330 aa.	Human Gene SWISSPROT- ID:P30542 ADENOSINE A1 RECEPTOR - HOMO SAPIENS (HUMAN), 326 aa.	Human Gene SWISSPROT- ID:P30542 ADENOSINE A1 RECEPTOR - HOMO SAPIENS (HUMAN), 326 aa.	Human Gene Homologous to SWISSPROT-ID:P31421 METABOTROPIC GLUTAMATE RECEPTOR 2 PRECURSOR - RATTUS NORVEGICUS (RAT), 872 aa.
tm7	tm7	tm7	tm7
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
H	-	O	O
O	ပ	ပ	⋖
GAATGTGGGGAT C AAGGCATTGGGA C[C/T]CTATCAGGT ATCCTGAGGAGA GACT	CAGCCGGGAGCT CTGCCAGCTTTGG [C/T]GAAGGAGGG TGCTTGCCTCGTG	CGGGAGCTCTGC CAGCTTTGGCGAA [G/C]GAGGGTGCT TGCCTCGTGCCC CTTG	TGCTCTTGCTGCT A GATGGAGGAGGA[A/GJGGGGTGGAT CCCGTGGAGCCT CCAA
76	135	139	1839
cg11751407 76	cg43326635	cg43326635	cg43993798
347	348	349	350

	1
Z.90E-74	2.90E-74
Human Gene Similar to SWISSPROT-ID:Q25322 TYRAMINE/OCTOPAMINE RECEPTOR 2 (TYR-LOC 2) - LOCUSTA MIGRATORIA (MIGRATORY LOCUST), 484 aa.lpcis:SPTREMBL-ID:Q25322 GCR2 (G PROTEIN-COUPLED RECEPTOR) - LOCUSTA MIGRATORIA (MIGRATORY	Human Gene Similar to SWISSPROT-ID:Q25322 TYRAMINE/OCTOPAMINE RECEPTOR 2 (TYR-LOC 2) - LOCUSTA MIGRATORIA (MIGRATORY LOCUST), 484 aa. Ipcls:SPTREMBL-ID:Q25322 GCR2 (G PROTEIN-COUPLED RECEPTOR) - LOCUSTA MIGRATORIA (MIGRATORY LOCUST), 484 aa.
tm7	DDI tm7
SILENT- NONCODI NG	SILENT- NONCODI NG
O	F
⋖	O
ATGCTTCCCCCAA A CCCTAGGGATC[A/CJACACTTAAGA TAATTCGCCACTT CT	CCAACCCTAGGG AATCAACACTTAA[G/IJATAATTCGCC ACTTCTCCTCTTT CT
cg43040271 2130	cg43040271 2139
351	352

	5 (5q32)	5 (5q32)	5 (5q32)
2.90E-74	2.00E-58	2.00E-58	2.00E-58
Human Gene Similar to SWISSPROT-ID:Q25322 TYRAMINE/OCTOPAMINE RECEPTOR 2 (TYR-LOC 2) - LOCUSTA MIGRATORIA (MIGRATORY LOCUST), 484 aa. Ipcls:SPTREMBL-ID:Q25322 GCR2 (G PROTEIN-COUPLED RECEPTOR) - LOCUSTA MIGRATORIA (MIGRATORY	Human Gene Similar to SWISSPROT-ID:Q24563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	Human Gene Similar to SWISSPROT-ID: 024563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	Human Gene Similar to SWISSPROT-ID:Q24563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.
C- tm7	T- tm7 ODI	T- tm7 ODI	T- tm7
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG
⊢	U	O	9
O	F	ď	U
AGATAATTCGCCA CTTCTCCTCTT[C //]ICTCTGCTCCG CTCACGGCTTGCA G	CGCAGAGCCCCG CCGTGGGTCCGC C[T/C]GCTGAGGC GCCCCAGCCAG	CAGCGCCTTCTTG A CTGGCACCCAAT[A/G]GAAGCCATGC GCCGGACCACGA	TGGCCGGACCA CGACGTCACGCA G[C/G]AAAGGGAC GAGGTGTGGGTG GTGGG
2163	1668	1760	1793
cg43040271	cg43040273	cg43040273	cg43040273
353	354	355	356

5 (5q32)	5 (5q32)	5 (5q32)	12	12
	2.00E-58	2.00E-58	1.70E-177	1.70E-177
Human Gene Similar to SWISSPROT-ID:024563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	Human Gene Similar to SWISSPROT-ID:Q24563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	Human Gene Similar to SWISSPROT-ID:Q24563 DOPAMINE RECEPTOR 2 - DROSOPHILA MELANOGASTER (FRUIT FLY), 539 aa.	transcriptfac Human Gene SPTREMBL-ID:Q07279 TRANSCRIPTION FACTOR NF-E2 - MUS MUSCULUS (MOUSE), 373 aa.	transcriptfac Human Gene SPTREMBL-ID:Q07279 TRANSCRIPTION FACTOR NF-E2 - MUS MUSCULUS (MOUSE), 373 aa.
tm7	tm7	tm7	transcriptfac tor	transcriptfac tor
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- trai NONCODI tor NG	SILENT- tra NONCODI tor NG
U	4	4	 -	U
9	O	gap	gap	O
GCAGGTCTTCTTT GAAGGCCTATGG[G/C]AATGGCTACT CCAGCAACGGCA	ATTGTAGTACAAA TGACTCACTGCT[G/A]TAAAGCAGTT TTTCTACTTTTAAA G	ATAAACTTAGAAT AAAATTGTAAAA[g ap/A]TTGTATAGAG ATATGCAGAAGGA AG	AGGGTGGAACT GCTGATGGGATTT [gap/T]CCTTCATTC CCTTCTGATAAAG GTA	AGCCTCCCCAGA GACAACACCGGG A[G/C]CCTCATCTC TCTCCTCACCCTG TCTCCTCACCCTG
2767	2953	3053	1501	249
cg43040273 2767	cg43040273	cg43040273	cg43998970	cg43998970
357	358	359	360	361

		5 (5p15.3)	_
4.20E-158 8	6.90E-68	0	0
transcriptfac Human Gene SWISSNEW- ID:P23193 TRANSCRIPTION ELONGATION FACTOR S-II (TRANSCRIPTION ELONGATION FACTOR A) - HOMO SAPIENS (HUMAN), 301 aa. jpcls:SWISSPROT-ID:P23193 TRANSCRIPTION ELONGATION FACTOR S-II (TRANSCRIPTION ELONGATION FACTOR A) - HOMO SAPIENS (HUMAN), 301 aa.	transcriptfac Human Gene Similar to tor TREMBLNEW-ID:G2920821 TRANSCRIPTION FACTOR T-BOX 5 - HOMO SAPIENS (HUMAN), 518 aa.	Human Gene SWISSPROT- ID:Q01959 SODIUM-DEPENDENT DOPAMINE TRANSPORTER (DA TRANSPORTER) (DAT) - HOMO SAPIENS (HUMAN), 620 aa.	Human Gene SWISSPROT- ACC:P02545 LAMIN A (70 KD LAMIN) - Homo sapiens (Human), 664 aa.
transcriptfac tor	transcriptfac tor	transport	UNCLASSI
SILENT- trai	SILENT- trai	SILENT- NONCODI NG	SILENT- NONCODI NG
	O	U	<
U	4	F	gap
GTCTTCTCCGCGC C CCACCCCGCTGG[C/T]AAGGGGAAGT GGGCGAAGCTGG AGC	GGGCCGGGCAC TGCCCAGGAAGG GAAGICTCCGGGA GAGGGAGCCGGC	AGACGAAGACCC CAGGAAGTCATCC [T/C]GCAATGGGA GAGACACGAACA AACC	CCCACGCCTGCC AGGAGCAAGCCG A[gap/A]GAGCCAG CCGGCCGCGCA CTCCGA
2623	934	2030	237
cg43947199	cg43917396	cg40351913	cg43921289
362	363	364	365

9	0	٥١	1 (1p32)	(17911)
			0	0
CAL to sapiens nt).	Human Gene SPTREMBL- ACC:Q16084 P130 - HOMO SAPIENS (HUMAN), 1139 aa.	Human Gene SPTREMBL- ACC:Q16084 P130 - HOMO SAPIENS (HUMAN), 1139 aa.	Human Gene SWISSPROT- ACC:P42566 EPIDERMAL GROWTH FACTOR RECEPTOR SUBSTRATE SUBSTRATE 15 (PROTEIN EPS15) (AF-1P PROTEIN) - Homo sapiens (Human), 896 aa.	Human Gene SWISSPROT- ACC:P53675 CLATHRIN HEAVY CHAIN 2 (CLH-22) - Homo sapiens (Human), 1640 aa.
UNCLASSI	ASSI	ASSI	UNCLASSI FIED	UNCLASSI
SILENT- NONCODI NG	SILENT- UNCI NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- NONCODI NG	SILENT- NONCODI NG
9	O	o o	O	O
∢	O	A	A	A
AAACAAATAAGCC A CTTTTTACTGAC[A /G]ATGCACCCAAC CTTTTCAGCTGAA G	AGAGTCAAAAATC CAAGTTTGGATT[C /GJTAAGCAGCCTT GACAGTAATCACT G	AAGCAGCCTTGAC A AGTAATCACTGAIA /GJTGGTAGGGAAA AAAAGACAGTTGG	AGGCAAAAGCTCA A CAGTAAATGTATĮA ICJCCAGAACAGG GGCCTAAGTGAA GGT	CTGCTCCCANCTT CGCCAGCCTCCA[A/GJTGTACAACTT CCGCGTGTAGTG GGC
3196	1309	1336	2206	4893
cg43928515 3196	cg43955093	cg43955093	cg43925474	cg44014437
366	367	368	369	370

17 (17q11)	20 (20pter)	21 (21q22.1)	22 (22q13.1)
0	0	0	0
UNCLASSI Human Gene SWISSPROT- FIED ACC:P53675 CLATHRIN HEAVY CHAIN 2 (CLH-22) - Homo sapiens (Human), 1640 aa.	Human Gene SWISSPROT- ACC:P05060 SECRETOGRANIN I PRECURSOR (SGI) (CHROMOGRANIN B) - Homo sapiens (Human), 677 aa.	Human Gene SWISSNEW- ACC:Q13009 T-LYMPHOMA INVASION AND METASTASIS INDUCING PROTEIN 1 (TIAM1 PROTEIN) - Homo sapiens (Human), 1591 aa.	Human Gene SWISSPROT- ACC:P13866 SODIUM/GLUCOSE COTRANSPORTER 1 (NA(+)/GLUCOSE COTRANSPORTER 1) (HIGH AFFINITY SODIUM-GLUCOSE COTRANSPORTER) - Homo sapiens (Human), 664 aa.
UNCLASSI	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI
SILENT- UNC NONCODI FIED NG	SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- UNCI NONCODI FIED NG
9	∢	 -	F
CTGCTCCCAACTT A CGCCAGCCTCCA[A/G]TGTACAACTT CCGCGTGTAGTG GGC	CACTTCACTGAAA C GACACCATTTAT[C /A]TACCCAAGGGC AGAAAGTAGAACT	GATAGGACTCAAG C CTTATTTGGGAT[C /T]CTGATCAATTC TTTCTGATGTTGT	TACAGCCATCTGT C ACCTACTGGAGC[C/T]GCAGAAGGG AAGTCCACTCAGT CAC
5114	2242	1939	2416
cg44014448	cg43973129	cg43950657	cg43956384
371	372	373	374

X (Xp22.3)			10	۲
0	0	0		1.20E-280
Human Gene SWISSPROT- ACC:P23352 KALLMANN SYNDROME PROTEIN PRECURSOR (ADHESION MOLECULE-LIKE X-LINKED) - Homo sapiens (Human), 680 aa.	Human Gene TREMBLNEW- ACC:AAD23581 CULLIN 2 - HOMO SAPIENS (HUMAN), 745 aa.	Human Gene TREMBLNEW- ACC:AAD23581 CULLIN 2 - HOMO SAPIENS (HUMAN), 745 aa.	Human Gene TREMBLNEW- ACC:CAA08974 GUANINE NUCLEOTIDE-EXCHANGE FACTOR - HOMO SAPIENS (HUMAN), 548 aa.	Human Gene SWISSPROT- ACC:P38567 HYALURONIDASE PRECURSOR (EC 3.2.1.35) (SPERM SURFACE PROTEIN PH- 20) (SPERM ADHESION MOLECULE 1) - Homo sapiens (Human), 509 aa.
ASSI	UNCLASSI	UNCLASSI FIED	UNCLASSI	UNCLASSI
SILENT- UNCI NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG
⋖	F	—	F	₹
5	∢	∢	4	
AGCAGTGCAGCC (CCGGCGCGGGGGGGGGGGGGGGGGGGGGGGGG	GAGAAAAAGCATG / GTACCCAACCGA[ATJTTTCCACTTTT CAGCAATACTTCA C	TAAAGTTTTAAGA / AATGTCATAATGIA / TJCATGAGCTTGA AATATCTCTAGGC AATATCTAGGC A	AGCAAAGAAACAC, TGGCAGAATTCC[ATJGCATTTGCAA AATTCTAAGTTTT GG	AAATAAATGTTTT CATAGTCATTAC[T /A]CTTTACAATGG GAGTGCTAAAATT C
101	260	323	1121	366
cg43992229 101	cg44932392	cg44932392	cg43981656	cg44910613
375	376	377	378	379

7	2 (2p25)	
2.10E-258	7.00E-251	4.80E-213
LLITUS ET - HOMO	1.17) ian), 461	Human Gene SWISSPROT-ACC:P32754 4-HYDROXYPHENYLPYRUVATEDIOXYGENASE (EC 1.13.11.27) (4HPPD) (HPD) - Homo sapiens (Human), 392 aa.
UNCLASSI FIED	LASSI	LASSI
SILENT- NONCODI NG	SILENT- NONCODI NG	SILENT- UNC NONCODI FIED NG
gap	gap	
g	U	4
CAATGCATGAATC TGTACCCTTCGG[G/gapJAGGGCACT CACATGCCGCC CCAGC	TTGTTCATGATTT CTTGATGTTCCT[C /gap]TAATGGAAA CTAAGAGATGGAA	GCCGAGTCCGCT GGTGGCGGACC C[A/T]AGGGGAGC AGCCAGTAGGGA AGTTG
1643	1961	129
cg43929959	cg43950250	cg43064090
381	382	383
	cg43929959 1643 CAATGCATGAATC G gap SILENT- UNCLASSI Human Gene SPTREMBL- TGTACCCTTCGG[NONCODI FIED ACC:P78506 DIABETES MELLITUS G/gapjAGGGCACT NG TYPE I AUTOANTIGEN (ISLET CACATGCCGCC CELL AUTOANTIGEN P69) - HOMO CCAGC SAPIENS (HUMAN), 483 aa.	cg43929959 1643 CAATGCATGAATC G gap SILENT- NONCODI FIED Human Gene SPTREMBL- ACC:P78506 DIABETES MELLITUS ACC:P18506 DIABETES ACC:P18506 DIABETES ACC:P18506 DIABETES MELLITUS ACC:P18506 DIABETES

			6	
			4 (4q21.2)	വ
4.80E-213	4.80E-213	4 .80E-213	1.20E-177	4.20E-166
Human Gene SWISSPROT- ACC:P32754 4- HYDROXYPHENYLPYRUVATE DIOXYGENASE (EC 1.13.11.27) (4HPPD) (HPD) - Homo sapiens (Human), 392 aa.	Human Gene SWISSPROT- ACC:P32754 4- HYDROXYPHENYLPYRUVATE DIOXYGENASE (EC 1.13.11.27) (4HPPD) (HPD) - Homo sapiens (Human), 392 aa.	Human Gene SWISSPROT- ACC:P32754 4- HYDROXYPHENYLPYRUVATE DIOXYGENASE (EC 1.13.11.27) (4HPPD) (HPD) - Homo sapiens (Human), 392 aa.	Human Gene SWISSPROT- ACC:P30968 GONADOTROPIN- RELEASING HORMONE RECEPTOR (GNRH-R) - Homo sapiens (Human), 328 aa.	Human Gene SWISSNEW- ACC:Q16637 SURVIVAL MOTOR NEURON PROTEIN 1 - Homo sapiens (Human), 294 aa.
LASSI	UNCLASSI FIED	UNCLASSI	UNCLASSI FIED	UNCLASSI FIED
SILENT- UNCI NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- NONCODI FIED NG	SILENT- NONCODI FIED NG	SILENT- UNC NONCODI FIED NG
 -	O	O	O	deb
A	O	O	⋖	<u></u>
CCGAGTCCGCTG // GTGGGCGGACCC A[A/T]GGGGGAGCA GCCAGTAGGGAA GTTGG	GGGAGCAGCCAG TAGGGAGTTGG G[C/G]GAGTTCCA GAATCAGGGGGC GTGGC	TAATCGGGAGGG CTGGAGCAGAGG G[C/G]GGCCCCGC CGAGGGGCGTGG TCAGT	GATGCCAAAAAAA CAAAGGTGAGAAGAAGGCACAACACACACACACACACACA	GTCTTTTACAGAT GGTTTTTCAAAA[T /gapJAGAGTCCAG TAAAATATTTCAC ATT
130	157	61	3296	381
cg43064090 130	cg43064090	cg43064090	cg30490224	cg43924431
384	385	386	387	388

g	1 (1p22)			
	7.70E-158 1	4.90E-156 2	1.10E-150 6	1.90E-138 7
V- OMO a.	Human Gene SWISSNEW- ACC:P13726 TISSUE FACTOR PRECURSOR (TF) (COAGULATION FACTOR III) (THROMBOPLASTIN) (CD142 ANTIGEN) - Homo sapiens (Human), 295 aa.	Human Gene SPTREMBL- ACC:Q92600 PROTEIN INVOLVED IN SEXUAL DEVELOPMENT, COMPLETE CDS - HOMO SAPIENS (HUMAN), 299 aa.	Human Gene Homologous to TREMBLNEW-ACC:AAC69899 SACM21 - MUS MUSCULUS (MOUSE), 721 aa.	Human Gene Homologous to TREMBLNEW-ACC:AAD23440 LR8 - HOMO SAPIENS (HUMAN), 270 aa.
UNCLASSI FIED	UNCLASSI FIED	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- UNC NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- NONCODI NG
<u> </u>	o o	├	ပ	de6
U	⋖	O	—	<u></u> 5
CGTTGTTCCTAAT GTGGATCTACCA[C/TJCCCTGTGTTC ATCGAGATTCCGG TC	TGGGATTACAGGT GCGCACTACCAC[A/G]CCAAGCTAAT TTTGTATTTTTA G	CCTTCAGCACCCC TGCAGCGGAAAAI CTJAATGAGCCGC CGTAGCCGCCAT CGTAGCCGCCAT	AAAAAGCTACAGA AAAGAAATCACTĮT ICJTGAAAAACACA ATGACTCAGAGG CA	CAGGGACATGCG GGCACCCCGTGG G[G/gap]TCTTTGG CGGCTCACAGGA CAATGG
607	1542	2065	176	418
cg43936047 607	cg43272443	cg43966848	cg43964140	cg43285114
389	390	391	392	393

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-		0
3.30E-125 11	2.70E-123	6.90E-118
.30E	70E	3.90
UNCLASSI Human Gene Homologous to FIED SWISSNEW-ACC:P18582 CD81 ANTIGEN (26 KD CELL SURFACE PROTEIN TAPA-1) - Homo sapiens (Human), 236 aa.	Human Gene Homologous to SPTREMBL-ACC:Q15025 MRNA (HA1652) FOR ORF, PARTIAL CDS - HOMO SAPIENS (HUMAN), 296 aa (fragment).	Human Gene Homologous to SWISSPROT-ACC:P22061 PROTEIN-L-ISOASPARTATE(D- ASPARTATE) O- METHYLTRANSFERASE (EC 2.1.1.77) (PROTEIN-BETA- ASPARTATE METHYLTRANSFERASE) (PIMT) (PROTEIN L- ISOASPARTYL/D- ASPARTYL METHYLTRANSFERASE) (L- ISOASPARTYL METHYLTRANSFERASE) - Homo Sapiens (Human), 226 aa.
UNCLASSI FIED	UNCLASSI	UNCLASSI FIED
SILENT- UNCI NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- UNC NONCODI FIED NG
gap	O	∢
C	4	<u></u>
GCAGGCAGAGCA G CCCTGGGACCCC A[G/gap]GGCAGAA GGACCCTGCCC	TAAACAGCTCAGT / TCAGGGACTGGT A/GJTACAAGCTGG CCACCATCTCAG CC	TTACAGGACATCA CCTGCCATCTTA[T /A]GGTTTAATATTT ACAAATGCCTAGT
370	649	259
cg43948566	cg44003626	cg43917206
394	395	396

	5	8	22 (22q12.1)
2.50E-111 8	2.90E-110 12	2.90E-110 12	1.20E-106 22 (22)
UNCLASSI Human Gene Homologous to SPTREMBL-ACC:000559 CANCER ASSOCIATED SURFACE ANTIGEN - HOMO SAPIENS (HUMAN), 213 aa.	Human Gene Homologous to SPTREMBL-ACC:P97314 DOUBLE LIM PROTEIN-1 - MUS MUSCULUS (MOUSE), 193 aa.	Human Gene Homologous to SPTREMBL-ACC:P97314 DOUBLE LIM PROTEIN-1 - MUS MUSCULUS (MOUSE), 193 aa.	Human Gene Homologous to SWISSPROT-ACC:P15018 LEUKEMIA INHIBITORY FACTOR PRECURSOR (LIF) (DIFFERENTIATION- STIMULATING FACTOR) (D FACTOR) (MELANOMA-DERIVED LPL INHIBITOR) (MLPLI) - Homo sapiens (Human), 202 aa.
UNCLASSI FIED	UNCLASSI FIED	ASSI	UNCLASSI
SILENT- UNCI NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- NONCODI FIED NG
i–	F	F	-
O	O	U	۲
GGCCGATTITTCC C ACAATTTAAATC[C //]CAGTTCACCTG GTATCCAGCTCCA	GTTTCCACCTCCC CAGACAGGCATT[C/TJCGAGTGGGA GGCGGGAGCACG TACC	TTTCCACCTCCCC AGACAGGCATTC[C/TJGAGTGGGAG GCGCGAGCACGT ACCG	CTAAACCCAAATG A GGGCCTGCTGGC[A/TIGACCCCGAG GGTGCCTGGCCA GTCC
	840	841	1030
cg43289666 215	cg43986282 8	cg43986282	cg43297716
397	398	399	400

	T		
8 (8922)			
7.90E-101 8 (8922)	1.00E-100	1.60E-100	1.60E-100
Human Gene Homologous to SWISSPROT-ACC:P34741 SYNDECAN-2 PRECURSOR (FIBROGLYCAN) (HEPARAN SULFATE PROTEOGLYCAN CORE PROTEIN) (HSPG) (SYND2) - Homo sapiens (Human), 201 aa.	Human Gene Similar to SPTREMBL- ACC:043399 HD54+INS2 ISOFORM - HOMO SAPIENS (HUMAN), 206 aa.	Human Gene Similar to SWISSNEW- 1.60E-100 ACC:P11686 PULMONARY SURFACTANT-ASSOCIATED PROTEIN C PRECURSOR (SP-C) (SP5) (PULMONARY SURFACTANT-ASSOCIATED PROTEOLIPID SPL(VAL)) - Homo sapiens (Human), 197 aa.	Human Gene Similar to SWISSNEW- 1.60E-100 ACC:P11686 PULMONARY SURFACTANT-ASSOCIATED PROTEIN C PRECURSOR (SP-C) (SP5) (PULMONARY SURFACTANT-ASSOCIATED PROTEOLIPID SPL(VAL)) - Homo sapiens (Human), 197 aa.
LASSI	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI
SILENT- UNCI NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG
<u> </u>	—	dap	O
TTTTATCATTAAAG C TGCCAGAATGG[C/ TJCTTTAATGAAA ACAAAAACAAAG	GGAGGGTTGGAG C TCACTGACGAATG [C/T]GAGCCGGGC CAGGCCCATGCA	GCCACCTGCCCG C GGCTGTGGAGGA G[C/gap]GCTCGCG CTGACCAGGCGC TGGGCG TGGGCGC	GCTTCTGCCCACA A CCGCAGGGACAA[A/G]CCCTGGAGAA ATGGGAGCNTGG GGA
2160	624	881	1124
cg43980312 2160	cg43939240 e	cg43941552 E	cg43941552
401	402	403	404

		_		
	52	10	10	10
2.10E-100 12	5.30E-95	3.40E-93	3.40E-93	3.40E-93
Human Gene Similar to SWISSPROT-ACC:P45973 HETEROCHROMATIN PROTEIN 1 HOMOLOG ALPHA (HP1 ALPHA) (ANTIGEN P25) - Homo sapiens (Human), 191 aa.	Human Gene Similar to SWISSPROT-ACC:P30536 PERIPHERAL-TYPE BENZODIAZEPINE RECEPTOR (PBR) (PKBS) (MITOCHONDRIAL BENZODIAZEPINE RECEPTOR) - Homo sapiens (Human), 169 aa.	Human Gene Similar to SWISSPROT-ACC:P36405 ADP- RIBOSYLATION FACTOR-LIKE PROTEIN 3 - Homo sapiens (Human), 182 aa.	Human Gene Similar to SWISSPROT-ACC:P36405 ADP- RIBOSYLATION FACTOR-LIKE PROTEIN 3 - Homo sapiens (Human), 182 aa.	Human Gene Similar to SWISSPROT-ACC:P36405 ADP- RIBOSYLATION FACTOR-LIKE PROTEIN 3 - Homo sapiens (Human), 182 aa.
LASSI	UNCLASSI	UNCLASSI FIED	LASSI	UNCLASSI
SILENT- UNC NONCODI FIED NG	SILENT- NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG
F	<u> </u>	∢	O	<u> </u>
O	ව	O	4	O
CATITCTCTTIGI ACATAATACATT[C MJACCTCCCTGCC TCCTCCTTTCT A	CAGGGGTCAGCA GAGCTTCAGAGG TG/TGCCCCACC TGAGCCCCCACC CGGGA	CAGAAAGCAGCA AATTAGTGTTTT[C/AJAGGACCGAAT TCGGCTCCCGCA	AAGCAGCAAATTA GTGTTTTCAGG[A ICCGGAATTCGGC TCCGCAGCTCCT	CTCCCGCAGCTC CTGCATCTCCATT[C/T]GTCTAGATTT TATTTCTTCTTTGC A
914	878	507	511	547
cg42917153	cg43927693	cg43951338	cg43951338	cg43951338
405	406	407	408	409

7.20E-91	7.20E-91	7.20E-91	7.20E-91
Human Gene Similar to SWISSNEW- 7.20E-91 ACC:P01185 VASOPRESSIN- NEUROPHYSIN 2-COPEPTIN PRECURSOR [CONTAINS: ARG- VASOPRESSIN; NEUROPHYSIN 2 (NEUROPHYSIN-II); COPEPTIN] - Homo sapiens (Human), 164 aa.	Human Gene Similar to SWISSNEW- 7.20E-91 ACC:P01185 VASOPRESSIN- NEUROPHYSIN 2-COPEPTIN PRECURSOR [CONTAINS: ARG- VASOPRESSIN; NEUROPHYSIN 2 (NEUROPHYSIN-II); COPEPTIN] -	Human Gene Similar to SWISSNEW-ACC:P01185 VASOPRESSIN-NEUROPHYSIN 2-COPEPTIN PRECURSOR [CONTAINS: ARGVASOPRESSIN; NEUROPHYSIN 2 (NEUROPHYSIN-II); COPEPTIN] - Homo sapiens (Human), 164 aa.	Human Gene Similar to SWISSNEW- 7.20E-91 ACC:P01185 VASOPRESSIN- NEUROPHYSIN 2-COPEPTIN PRECURSOR [CONTAINS: ARG- VASOPRESSIN; NEUROPHYSIN 2 (NEUROPHYSIN-II); COPEPTIN] - Homo sapiens (Human), 164 aa.
SILENT- UNCLASSI NONCODI FIED NG	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- NONCODI NG	SILENT- NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- UNC NONCODI FIED NG
—	-	—	F
gap	O	O	O
CCCGCCCAGCCC g GACGCCTACTGA G[gap/T]CCCCGCG CTCGCCCCACCG GCGCGC	CCAGCCCGACGC CTACTGAGCCCC G[C/T]GCTCGCCC CACCGCGCGCGT CTTCG	AGCCGACGCCT GACTGAGCCCCGC GIC/ITCGCCCCACGCGCCTCT TCGCCCTTTCGCCCTTTCGCCCTCTTCGCGCGCTCTTCGCG	CGACGCCTACTG AGCCCCGCGCTC G[C/T]CCCACCGG CGCGCTCTTCGC GCCCC
1234	1240	1242	1246
cg25236776 1234	cg25236776	cg25236776	cg25236776
410	411	412	413

X (Xp11.4)	11 (11p15.2)	_	-	~
5.00E-83 X	2.00E-70	1.60E-67	4.30E-66	4.30E-66
Human Gene Similar to REMTREMBL-ACC:E47283 DNA FOR ORF1 AND ORF2 FROM CHROMOSOME X - HOMO SAPIENS (HUMAN), 157 aa.	Human Gene Similar to SWISSNEW- 2.00E-70 ACC:P01258 CALCITONIN PRECURSOR - Homo sapiens (Human), 141 aa.	Human Gene Similar to TREMBLNEW-ACC:AAD39844 HSPC028 - HOMO SAPIENS (HUMAN), 419 aa.	Human Gene Similar to TREMBLNEW-ACC:AAD29427 MYOMEGALIN - RATTUS NORVEGICUS (RAT), 2324 aa.	Human Gene Similar to TREMBLNEW-ACC:AAD29427 MYOMEGALIN - RATTUS NORVEGICUS (RAT), 2324 aa.
SILENT- UNCLASSI NONCODI FIED NG	UNCLASSI	UNCLASSI	UNCLASSI	UNCLASSI
SILENT- NONCODI NG	SILENT- NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG	SILENT- UNCI NONCODI FIED NG
4	—	gap	gap	gap
yap	O	 -	4	A
GCTACGTTTACTC gap ACAGCCAGCGAA[gap/A]CTGACATTA AAATAACTAACAA ACA	CGCCTCTGATCCA AGCCACCTCCCG C/TJCAGAGAGGTG TCATGGGCTTCCA AA	CTCTGCACAAGG GAAGCCTATCCTA [T/gap]TTTTTTTT CCTTTGCGAAAAC AGA	AATGCCTCAGATC AGTGAGG AGTGAGG AGADJACCTTCCAGATGGATGAATA GACTGAAATA GAC	ATGCCTCAGATCA GTGACCCAAGGA[A/gap]CCTTCCAGA ATGGATGAAATAG ACC
1362	104	356	1119	1120
cg43968406	cg42748886	cg43969533	cg43976681 1119	cg43976681
414	415	416	417	418

0	9 (9q22)		~
	6.60E-65	5.90E-64	2.00E-54
SILENT- UNCLASSI Human Gene Similar to SPTREMBL- 7.30E-66 NONCODI FIED ACC:O00455 TTF-I INTERACTING NG PEPTIDE 20 - HOMO SAPIENS (HUMAN), 385 aa (fragment).	Human Gene Similar to SWISSPROT-ACC:P05062 FRUCTOSE-BISPHOSPHATE ALDOLASE B (EC 4.1.2.13) (LIVER- TYPE ALDOLASE) - Homo sapiens (Human), 363 aa.		Human Gene Similar to SWISSNEW- 2.00E-54 ACC:P47992 LYMPHOTACTIN PRECURSOR (CYTOKINE SCM-1) (ATAC) (LYMPHOTAXIN) (SCM-1- ALPHA) - Homo sapiens (Human), 114 aa.
UNCLASSI	UNCLASSI	UNCLASSI FIED	UNCLASSI
SILENT- UNCI NONCODI FIED NG	SILENT- UNC NONCODI FIED NG	SILENT- NONCODI NG	SILENT- UNCI NONCODI FIED NG
—	V V	A	O
O	Ø	O	O
CCAAGCGGAAGG (CCATTTCCCTGC) CMJCTTCCTCAGT TGTCCGGGGCGG	CTAATTGTGTCGA ATTTCCAGGATTG /AJGAGGAAAAGTT GCTCCCTTTCAGC C	AAAGCAATCACAG G TGTTAAAAGAAG[G/a]CACGTTGAAA TGATGCAGGCTG	CCAGCCAGCTCAT G TTCACTTTACAC[G /C]CTCATGGACTG AGTTTATACTCAC C
714	398	577	423
cg43984044 714	cg43933283	cg42381630	cg41664708 423
419	420	421	422

13 (13q14.3)	17 (17q21.3 2)	17 (17q21.3 2)	17 (17q21.3 2)
0	0	o	0
Human Gene SWISSPROT- ID:P35670 COPPER- TRANSPORTING ATPASE 2 (EC 3.6.1.36) (COPPER PUMP 2) (WILSON DISEASE-ASSOCIATED PROTEIN) - HOMO SAPIENS (HUMAN), 1465 aa.	Human Gene SWISSPROT- ID:P08514 PLATELET MEMBRANE GLYCOPROTEIN IIB PRECURSOR (GPIIB) (INTEGRIN ALPHA- IIB) (CD41) - HOMO SAPIENS (HUMAN), 1039 aa.	BRANE JRSOR IIB)	Human Gene SWISSPROT- ID:P08514 PLATELET MEMBRANE GLYCOPROTEIN IIB PRECURSOR (GPIIB) (INTEGRIN ALPHA- IIB) (CD41) - HOMO SAPIENS (HUMAN), 1039 aa.
CONSER ATPase_as	cadherin	cadherin	cadherin
CONSER	CONSER	CONSER VATIVE	CONSER
Val (652)	Gly (653)	Asp (654)	Asp (655)
Ala	Ala	Glu	Asn
<u> </u>	ڻ ا	O	O
<u></u> 0	O	O	A
AGCCTTCCCGCA GAAAAGATGCAG [C/T]CCCCCAGAC CTTCTCTGTGCTG ATT	TACCAGAGGCTG CATCGGCTGCGC G[C/G]AGAGCAGA TGGCGTCGTATTT TGGG	TGGTGGCGCTC CACTGTATATGGA [G/CJAGCCGGGCA GACCGAAAACTG GCCG	CTCTCAACAGGCA A GGCACCACCCTG[A/GJACCTGGATCT GGGCGGAAAGCA CAG
3906	1138	1238	1893
cg43277632	cg40310734	cg40310734	cg40310734
423	424	425	426

9 (9p24)	(11923)	17 (17q25.2)	17 (17q25.2)
0	1.80E-203	7.40E-199	7.40E-199 17 (17
Human Gene SWISSPROT- ID:P98155 VERY LOW-DENSITY LIPOPROTEIN RECEPTOR PRECURSOR (VLDL RECEPTOR) - HOMO SAPIENS (HUMAN), 873 aa.	Human Gene SWISSNEW- ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa.lpcls:SWISSPROT-ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa.	glucoamylas Human Gene TREMBLNEW- ID:G2826521 MALTASE- GLUCOAMYLASE (EC 3.2.1.20) - HOMO SAPIENS (HUMAN), 1857 aa.	glucoamylas Human Gene TREMBLNEW- e ID:G2826521 MALTASE- GLUCOAMYLASE (EC 3.2.1.20) - HOMO SAPIENS (HUMAN), 1857 aa.
hde	eph	glucoamylas e	glucoamylas e
CONSER eph VATIVE	CONSER	CONSER VATIVE	CONSER
Ala (656)	Lys (657)	Arg (658)	Arg (659)
Gly	Arg	I.S.	Ξ S
O	⋖	<u>o</u>	O
O	O	A	⋖
GGTTACAAGTGTG G AATGTAGTCGTG[G/CJCTATCAAATG GATCTTGCTACTG GC	GCCGAGGACGTG CGTGGCAACCTG A[G/A]GGGCAACA CCGAGGGGCTGC AGAAG	TACGAGGTGCCC TTGGAGACCCGG C[A/G]TGTCCACA GCCGGGCACCGT CCCCA	GAGGAGCCCTTC GGGGTGATCGTG C[A/G]CCGGCAGC TGGACGGCCGCG
1883	949	1036	1108
cg43982507	cg41554010	cg43299024	cg43299024
427	428	429	430

01		14 (14q11.2)	2 (2q21)
0	6.40E-91	9.90E-70	0
CONSER glycoprotein Human Gene SWISSPROT- LIPOPROTEIN RECEPTOR- RELATED PROTEIN 2 (MEGALIN) (GLYCOPROTEIN 330) - HOMO SAPIENS (HUMAN), 1751 aa (fragment).	glycoprotein Human Gene Similar to SWISSPROT-ID:P38159 HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN G (HNRNP G) (GLYCOPROTEIN P43) - HOMO SAPIENS (HUMAN), 437 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P16452 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.	Human Gene SWISSPROT- ID:P09848 LACTASE-PHLORIZIN HYDROLASE PRECURSOR (EC 3.2.1.108) (EC 3.2.1.62) (LACTASE- GLYCOSYLCERAMIDASE) - HOMO SAPIENS (HUMAN), 1927 aa.
glycoprotein	glycoprotein	glycoprotein	hydrolase
CONSER	CONSER	CONSER	CONSER
Leu (660)	Arg (661)	(662)	(663)
<u>e</u>	H Si	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	<u>=</u>
O	O	<	O
A	A	ڻ ن	∢
GACTGACTGGGG AAAGGAACCTAAA [A/C]TCGAGTCTG CCTGGATGAATG GAGA	AGTTATTCTAGAG AGTACAGAATCI AGITCGAAGTTCC CGAGAAACTAGG GAG	GGACCAGGGGGC CATGCTGCTCAAT [G/A]TCTCAGGCC ACGTCAAGGAGA GCGG	TGCTTTTCAGGGC A GGAAAACTCTCT[A/G]TTGTCCTGCG AGCTGAAGATATC CC
12840	1004	2101	999
cg43285373	cg36834323	cg41568631	cg42359655
431	432	433	434

16 (16q22)	18 (18q21.3)
2.00E-220 16 (16	2.20E-149 18 (18 (18)
Leu CONSER hydroxyster Human Gene SPTREMBL- ID:Q13194 11-BETA- ID:Q13194 11-BETA- HYDROXYSTEROID DEHYDROGENASE TYPE 2 - HOMO SAPIENS (HUMAN), 405 aa.	CONSER immunoglob Human Gene Homologous to VATIVE SPTREMBL-ID:P91456 SIMILAR TO THE IMMUNOGLOBULIN SUPERFAMILY - CAENORHABDITIS ELEGANS, 1173 aa.
hydroxyster oid	dolgonnmmi
CONSER	CONSER
Leu (664)	Phe (665)
\ 	Tyr
∢	—
U	4
GTGTGGCCCTTG C GTGAACTCTAGCA [C/A]GCGGCTAAT GTCCTGGTTTG GTC	GGAGATGTGGTC A ATTCCTAGTGATT[ATJTTTCAGATA GTGGGAGGAAGC AAC
	1133
cg43998672 1331	cg43969028 1133
435	436

	10
2.50E-206	0
Human Gene SWISSNEW- ID:P29466 INTERLEUKIN-1 BETA CONVERTASE PRECURSOR (IL- 1BC) (EC 3.4.22.36) (IL-1 BETA CONVERTING ENZYME) (ICE) (INTERLEUKIN-1 BETA CONVERTING ENZYME) (P45) (CASPASE-1) (CASP-1) - HOMO SAPIENS (HUMAN), 404 aa. pols:SWISSPROT-ID:P29466 INTERLEUKIN-1 BETA CONVERTING ENZYME) (ICE) (INTERLEUKIN-1 BETA CONVERTING ENZYME) (ICE) (INTERLEUKIN-1 BETA CONVERTING ENZYME) (ICE) (CASPASE-1) (CASP-1) - HOMO SAPIENS (HUMAN), 404 aa.	Human Gene SWISSNEW- ID:P33176 KINESIN HEAVY (UBIQUITOUS KINESIN HEAVY CHAIN) (UKHC) - HOMO SAPIENS (HUMAN), 963 aa. pcls:SWISSPROT-ID:P33176 KINESIN HEAVY CHAIN (UBIQUITOUS KINESIN HEAVY CHAIN) (UKHC) - HOMO SAPIENS (HUMAN), 963 aa.
VATIVE interleukin	kinesin
CONSER	CONSER
(666)	Leu (667)
<u>합</u>	
ပ	⋖
⋖	U
AAGGAGAAGAGA AAGCTGTTTATCC A/GJTTCCATGGGT GAAGGTACAATAA AT	GCCACTGTCTCTT CCAAACCCTTCA[C/A]GCCTTGTCTT GCTTGTTCTCGTC TA
133	1163
cg43933479	cg43942537
437	438

O	o	တ	(11922)
	1.80E-113 19	1.80E-113 19	0
Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene SWISSNEW- ID:P06401 PROGESTERONE RECEPTOR (PR) - HOMO SAPIENS (HUMAN), 933 aa. pcls:SWISSPROT-ID:P06401 PROGESTERONE RECEPTOR (PR) - HOMO SAPIENS (HUMAN), 933 aa.
MHC	MHC	MHC	nucl_recpt
CONSER MHC	CONSER VATIVE	CONSER	CONSER
lle (668)	Leu (669)	Asp (670)	(671)
Val	Vai	Asn	\all
∢	U	©	F
<u>ග</u>	O	∢	9
TTCCAAATGCTGA G GCCCAGAGCGTT[G/A]TCTCCTGCCC ATGAGCACCACA	CTGGAACAGTTTC CTCATTAGCCCT[G/C]TGACCCCAG CACACGCAGGGA CCTA	TCATCGCTGGTGC A TCCAAAAAAAAA /GJATGCTGCTGTA ATGAACCAAGAGC	GGATGCTGTTGCT CTCCCACAGCCA[G/T]TGGGCGTTCC AAATGAAAGCCAA GC
1035	271	823	3434
cg38337333	cg38337333	cg38337333	cg30421838
439	440	441	442

22	3 (3p21.3)	15	12
4.10E-254 22		1.10E-97	1.10E-97
Human Gene SWISSPROT- ID:Q07869 PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR ALPHA (PPAR-ALPHA) - HOMO SAPIENS (HUMAN), 468 aa. pcls:SPTREMBL-ID:Q16241 PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR ALPHA - HOMO SAPIENS (HUMAN), 468 aa (fragment).	Human Gene SWISSPROT- ID:P40692 MUTL PROTEIN HOMOLOG 1 (DNA MISMATCH REPAIR PROTEIN MLH1) - HOMO SAPIENS (HUMAN), 756 aa.	Human Gene Similar to SWISSPROT-ID:P01118 TRANSFORMING PROTEIN P21/K- RAS 2B - HOMO SAPIENS (HUMAN), 188 aa.	Human Gene Similar to SWISSPROT-ID:P01118 TRANSFORMING PROTEIN P21/K- RAS 2B - HOMO SAPIENS (HUMAN), 188 aa.
nucl_recpt	nuclease	oncogene	oncogene
CONSER nucl_recpt	CONSER	CONSER	CONSER VATIVE
(672)	Val (673)	Glu (674)	Gln (675)
Ala	<u>e</u>	Glu	Olu Olu
H	O	O	U
O	F	O	9
GCCAATGGCATC CAGAACAAGGAG GC/TJGGAGGTCC GCATCTTTCACTG CTGC	TCTCGACTAACAG CATTTCCAAAGA[T /C]GGAGCGAATAT TGTCCACGGTTGA G	GAGTGCCTTGAC GATACAGCTAATT[C/GJAGAATCATTT TGTGGACGAATAT GA	AAGAAGTTATGGA ATTCCTTTTATT[G/ CJAAACATCAGCA AAGACAAGACAG GG
1019	1860	194	548
cg43064060	cg43991813	cg42904626	cg42904626
443	444	445	446

3 (3p14.2)	19	(((((((((((((((((((
0	1.40E-79	0
	REMBL- S ACID SCULUS	Human Gene SWISSNEW- ID:P25205 DNA REPLICATION LICENSING FACTOR MCM3 (DNA POLYMERASE ALPHA HOLOENZYME-ASSOCIATED PROTEIN P1) (RLF BETA SUBUNIT) (P102 PROTEIN) - HOMO SAPIENS (HUMAN), 808 aa.[pcis:SWISSPROT-ID:P25205 DNA REPLICATION LICENSING FACTOR MCM3 (DNA POLYMERASE ALPHA HOLOENZYME-ASSOCIATED PROTEIN P1) (RLF BETA SUBUNIT) (P102 PROTEIN) - HOMO SAPIENS (HUMAN), 808 aa.
phosphatas e	phosphatas e	polymerase
CONSER	CONSER	VATIVE
(676)	Ala (677)	(678)
Ala	\ \ al	ren
<u> </u>	O	O
O	H	O
GCCGCCTCAGCC AGCAAGCAGGCG G[C/T]TAGGCCAG TCCTAGCCACCAC AGAG	GGGATGTACTGC ATGGTGTTCTTGG [T/C]GCTGTATGTG CAGGCACGACTC TGT	TCAGGTGGTGGG AACCTACCGTTGC [C/G]TTCCTGGAA AGAAGGGAGGCT ACAC
2845	582	807
cg42460457 2845	cg43272594	cg43958858
447	448	449

7 (7q21.3)	ω	12 (12q24.2)	12 (12q24.2)
1.20E-247 7 (7	0	0	0
OMO	Human Gene SWISSPROT- ID:P54296 M-PROTEIN (165 KD TITIN-ASSOCIATED PROTEIN) (165 KD CONNECTIN- ASSOCIATED PROTEIN) - HOMO SAPIENS (HUMAN), 1465 aa.	Human Gene SWISSPROT- ID:P29475 NITRIC-OXIDE SYNTHASE, BRAIN (EC 1.14.13.39) (NOS, TYPE I) (NEURONAL NOS) (NNOS) - HOMO SAPIENS (HUMAN), 1434 aa.	Human Gene SWISSPROT-ID:P29475 NITRIC-OXIDE SYNTHASE, BRAIN (EC 1.14.13.39) (NOS, TYPE I) (NEURONAL NOS) (NNOS) - HOMO SAPIENS (HUMAN), 1434 aa.
protease	struct	synthase	synthase
CONSER protease	CONSER VATIVE	CONSER	CONSER
Ser (679)	(680)	(681)	Ala (682)
Thr	Asn	Val	Gly
<u> -</u>	9	O	O
⋖	4	O	O
GTACAGCGGGCG A GGCCACCTCGGG C[AT]CTGAGCAC CAATTTGCGGGG GGCG	GGATGCTGGAGA GTGGATCACTGTC [A/G]ATCAGACGA CAACAGCCAACC GTTA	GATTCCTCCAGAG G CTGGTGTTGGAA[G/GTTCCCATCAG GCACCCCAAGTTT GA	AAGTTTGAGTGGT G TCAAGGACCTGG[G/G]CTGAAGTG GTACGGCCTCCC CGCC
540	2745	2337	2380
cg43916732 540	cg42894809	cg40388639	cg40388639
450	451	452	453

9	9
7.70E-79	7.70E-79
Human Gene Similar to SWISSNEW- 7.70E-79 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL- ACTIVATING ENZYME) (ACETYL- COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa. pcls:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL- ACTIVATING ENZYME) (ACETYL- COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.	Human Gene Similar to SWISSNEW- 7.70E-79 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATE-COA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.pcis:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATE-COA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA LIGASE) (ACYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.
CONSER synthase	synthase
CONSER VATIVE	CONSER
Gly (683)	(684)
Ala	년 년
<u>ග</u>	<u> </u>
O	∢
AATTTCTATATCA CTGGGGACAGAG[C/GJATATATGGAT AAAGATGGGTATT TC	TGGAACAAGTGG ATATCCGAAAATG[ATJCTGCACACAC CCACAGCAGTTTT GG
1524	698
cg43124627	cg43124627
454	455

		3 (3q21)	ω
7.40E-65	7.00E-172	1.20E-55	5.50E-89
Human Gene Similar to SWISSNEW- 7.40E-65 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA VITHASE) - BACILLUS SUBTILIS, 572 aa.jpcls:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATECOA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA LIGASE) SUBTILIS, 572 aa.	Human Gene SWISSPROT- ID:P33032 MELANOCORTIN-5 RECEPTOR (MC5-R) (MC-2) - HOMO SAPIENS (HUMAN), 325 aa.	Human Gene Similar to SPTREMBL- ID:Q89609 G PROTEIN-COUPLED RECEPTOR - EQUINE HERPESVIRUS TYPE 2 (EHV-2), 383 aa.	Human Gene Similar to TREMBLNEW-ID:G2653845 TNF RECEPTOR-RELATED RECEPTOR FOR TRAIL - HOMO SAPIENS (HUMAN), 386 aa.
synthase	tm7	tm7	tnfreceptor
CONSER	CONSER VATIVE	CONSER	CONSER
(685)	Phe (686)	Tyr (687)	Val (688)
\sqrt{a}	Tyr	Phe	Ala
⋖		<u> </u>	-
O	∢	⋖	U
AGGAGAGGTGGT GAAGGCATTTGTG [G/A]TCCTGGCCT CGCAGTTCCTGTC CCA	GTGATGGACCCT CTCATATATGCCT[A/T]CCGCAGCCAA GAGATGCGGAAG ACC	TTCCATCTGAGGT TTATAAACCACG[A /TJATTCAGGCAAA GTGGCCAGAATG GC	CAAGACCTAGCTC CCCAGCAGAGAGI C/TJGGCCCCACAA CAAAAGAGGTCCA
1464	1090	964	344
cg43064068	cg2514276	cg32423505	cg43335558
456	457	458	459

27.	9 (9q34)
1.70E-177 12	6.50E-192 9 (9q34)
CONSER transcriptfac Human Gene SPTREMBL- VATIVE tor ID:Q07279 TRANSCRIPTION FACTOR NF-E2 - MUS MUSCULUS (MOUSE), 373 aa.	Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B SAPIENS (HUMAN), 354 aa.
transcriptfac tor	transferase
CONSER	CONSER
Glu (689)	(690)
Gli	ĠĠ
O	O
O	O
GACAGAGCTGTA C CCGTGACATTTTC[C/GJAGCACCTTCG GGATGAATCAGG	GAGGGCGATTTCT ACTACCTGGGGG[G/C]GTTCTTCGGG GGGTCGGTGCAA GAG
	008
cg43998970 1347	cg2537639
460	191

ဖ	6 (6p21.3)	တ	4
0	0	0	0
Human Gene SWISSPROT- ID:Q03518 ANTIGEN PEPTIDE TRANSPORTER 1 (APT1) (PEPTIDE TRANSPORTER TAP1) (PEPTIDE TRANSPORTER PSF1) (PEPTIDE SUPPLY FACTOR 1) (PSF-1) (PEPTIDE TRANSPORTER INVOLVED IN ANTIGEN PROCESSING 1) - HOMO SAPIENS (HUMAN), 748 aa.	Human Gene SPTREMBL- ID:Q28437 ABC-TRANSPORTER - GORILLA GORILLA (LOWLAND GORILLA), 703 aa.	Human Gene SPTREMBL- ACC:O14914 NEURONAL MUNC18- 1 BINDING PROTEIN - HOMO SAPIENS (HUMAN), 837 aa.	Human Gene SWISSPROT- ACC:P29374 RETINOBLASTOMA BINDING PROTEIN 1 (RBBP-1) - Homo sapiens (Human), 1257 aa.
transport	transport	UNCLASSI FIED	UNCLASSI FIED
CONSER transport	CONSER VATIVE	CONSER	CONSER
Val (691)	(692)	Val (693)	Val (694)
<u>⊕</u>	Val	Ala	Leu
O	∢	<u> </u>	O
∢	<u>ග</u>	U	o o
AGTGTCCCTCACC A ATGGTCACCCTG[A/G]TCACCCTGCC TCTGCTTTTCCTT CT	CCTGGAACGCGC CTTGTACCTGCTC IG/AJTAAGGAGGG TGCTGCACTTGG GGGT	GAGCACGAGGAA GCCATGAATGCG GC/TICTACTCAG GCTACGTCTACAC	AGATACTITICTAT AAGCAGTTITTA[G ICJATTGTAGGAAG CAGCTGAATTCAA A
1552	1424	730	3568
cg43935995	cg43935986	cg43968274	cg44018598
462	463	464	465

ro.	_	1 (1942)	22 (22q11.2)	6 (6q23)
0 16				1.30E-171 6
Human Gene SWISSPROT- ACC:Q15046 LYSYL-TRNA SYNTHETASE (EC 6.1.1.6) (LYSINETRNA LIGASE) (LYSRS) (KIAA0070) - Homo sapiens (Human), 597 aa.	Human Gene SWISSPROT- ACC:P42694 HYPOTHETICAL PROTEIN KIAA0054 - Homo sapiens (Human), 1942 aa.	Human Gene SWISSPROT- ACC:P01019 ANGIOTENSINOGEN PRECURSOR - Homo sapiens (Human), 485 aa.	Human Gene SWISSPROT- ACC:P20062 TRANSCOBALAMIN II PRECURSOR - Homo sapiens (Human), 427 aa.	Human Gene SWISSPROT- ACC:P05089 ARGINASE 1 (EC 3.5.3.1) (LIVER-TYPE ARGINASE) - Homo sapiens (Human), 322 aa.
Unclassi Fied	UNCLASSI	UNCLASSI FIED	UNCLASSI	UNCLASSI
CONSER VATIVE	CONSER VATIVE	CONSER	CONSER	CONSER
Ser (695)	His (696)	(697)	(698)	(699)
Thr	Arg	- US	<u>=</u>	Glu
<u>ن</u>	<u> </u>	ග	ပ	ပ
ပ	0	U	4	U
ACACTGGAAAGCA C CAACAGTTGGCA[C/G]TTCTGTCTAG AAAATAATAATTG CA	AACGCTGCCCTG ACTGAGAAAGGC A[C/T]GATGCTCG CTCCACTGCTGGA	CATCCAGGACAAC C TTCTCGGTGACT[C/GJAAGTGCCCTT CACTGAGAGCGC CTG	CTTCAACCCTGGT CGGAGACAACGG A/CJTCACCATGGC CATCAGAACAGTG	CTGATTCTTCCGT TCTTCTTGACTT[C /GJTGCCACCTTGC CAGCCAGCTGCT CG
1825	1622	1381	996	1148
cg44926796	cg43055918	cg43966985	cg43918854	cg43918484
466	467	468	469	470

		6 (6q25.3)	
9.60E-148	9.60E-148	5.70E-124	7.20E-91
CONSER UNCLASSI Human Gene Homologous to VATIVE FIED SWISSNEW-ACC:Q12846 SYNTAXIN 4 - Homo sapiens (Human), 297 aa.	CONSER UNCLASSI Human Gene Homologous to VATIVE FIED SWISSNEW-ACC:Q12846 SYNTAXIN 4 - Homo sapiens (Human), 297 aa.	Human Gene Homologous to SWISSNEW-ACC:P04179 SUPEROXIDE DISMUTASE [MN] PRECURSOR (EC 1.15.1.1) - Homo sapiens (Human), 222 aa.	Human Gene Similar to SWISSNEW- 7.20E-91 ACC:P01185 VASOPRESSIN- NEUROPHYSIN 2-COPEPTIN PRECURSOR [CONTAINS: ARG- VASOPRESSIN; NEUROPHYSIN 2 (NEUROPHYSIN-II); COPEPTIN] - Homo sapiens (Human), 164 aa.
UNCLASSI	UNCLASSI FIED	UNCLASSI	UNCLASSI
CONSER VATIVE	CONSER	CONSER VATIVE	CONSER
Val (700)	Asp (701)	Gln (702)	Val (703)
Ala	Glu	n 9	Gi Gi
<u> </u>	—	O	<u> </u>
O	9	ග	ပ
ACGGCCCTGGAG C AACCAGAAGAAG GC/TJGAGGAAGA AGAAAGTCTTGAT TGCC	GGATGGTGTCTG ATGAGGAGTTGG A[G/T]CAGATGCT GGACAGTGGGCA AAGCG	TTGGGGTTGGCTT GGTTTCAATAAG G/CJAACGGGGAC ACTTACAAATTGC TGC	GTGACCGAGCCC GAGTGCCGCGAG G[G/T]CTTTCACC GCGCGCCCGCG CCAGC
1009	725	921	1094
cg43942977 1009	cg43942977	cg43943361	cg25236776
471	472	473	474

		۲		
7.20E-91	5.70E-75	1.30E-66	1.60E-54	1.60E-54
Human Gene Similar to SWISSNEW- 7.20E-91 ACC:P01185 VASOPRESSIN- NEUROPHYSIN 2-COPEPTIN PRECURSOR [CONTAINS: ARG- VASOPRESSIN; NEUROPHYSIN 2 (NEUROPHYSIN-II); COPEPTIN] -	Human Gene Similar to REMTREMBL-ACC:G292791 T- CELL RECEPTOR BETA PRECURSOR - HOMO SAPIENS (HUMAN), 145 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G2104755 T CELL RECEPTOR V-BETA 23 - HOMO SAPIENS (HUMAN), 129 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).
CONSER UNCLASSI VATIVE FIED	UNCLASSI FIED	UNCLASSI	UNCLASSI	UNCLASSI
CONSER	CONSER	CONSER	CONSER VATIVE	CONSER
Val (704)	Leu (705)	His (706)	lle (707)	Asp (708)
Gly	Val	Arg	Val	Glu
	O	∢	∢	O
Ð	O	O	O	O
CAGTGCCTCCCCT GCGGCCCGGGG [G/T]CAAAGGCCG CTGCTTCGGGCC CAGC	GGCCAACTCTGCT ATGGACACCAGA G/CJTACTCTGCTG TGCGGTCATCTGT CT	GCCTGGAACACC AGGCTCCTCTGC C[G/A]TGTCATGCT TTGTCTCCTGGGA GCA	AGCCACCCAGAC CGGAGACTCGGC C[G/A]TCTACCTCT GTGCTGTGGAGG	CGGCCGTCTACC TCTGTGCTGTGGA [G/C]GCCTATTCTA ACGACTACAAGCT CA
881	30	253	519	539
cg25236776	cg38899722	cg11753818	cg2526759	cg2526759
475	476	477	478	479

	13 (13q14.3)
2.10E-52	0
CONSER UNCLASSI Human Gene Similar to SWISSPROT-ACC:P01286 SOMATOLIBERIN PRECURSOR (GROWTH HORMONE-RELEASING FACTOR) (GRF) (GROWTH HORMONE-RELEASING HORMONE) (GHRH) (SOMATOCRININ) - Homo sapiens (Human), 108 aa.	ATPase as Human Gene SWISSPROT- sociated TRANSPORTING ATPASE 2 (EC 3.6.1.36) (COPPER PUMP 2) (WILSON DISEASE-ASSOCIATED PROTEIN) - HOMO SAPIENS (HUMAN), 1465 aa.
UNCLASSI	
CONSER	NON- CONSER VATIVE
Asp (709)	Gly (710)
<u>n</u>	Arg
H	Ø
O	4
CAGAACAAAAGCA G AATGGAATTGGA[G/TJAGCATCCTGG TGGCCCTGCTGC AGA	GAAACCCGGAAG CACTGTAATTGCG [A/G]GGTCTATAAA TGCACATGGCTCT GT
368	3110
cg1902363	cg43277632 3110
480	481

× (Xq12)	3 (3q21)	17 (17q21.3 2)
0	8.20E-288 3 (3q21)	0
Human Gene SWISSNEW- ID:Q04656 COPPER- TRANSPORTING ATPASE 1 (EC 3.6.1.36) (COPPER PUMP 1) (MENKES DISEASE-ASSOCIATED PROTEIN) - HOMO SAPIENS (HUMAN), 1500 aa.[pcls:SWISSPROT-ID:Q04656 COPPER-TRANSPORTING ATPASE 1 (EC 3.6.1.36) (COPPER PUMP 1) (MENKES DISEASE-ASSOCIATED PROTEIN) - HOMO SAPIENS (HUMAN), 1500 aa.	Human Gene SWISSPROT- ID:P05166 PROPIONYL-COA CARBOXYLASE BETA CHAIN PRECURSOR (EC 6.4.1.3) (PCCASE) (PROPANOYL- COA:CARBON DIOXIDE LIGASE) - HOMO SAPIENS (HUMAN), 539 aa.	Human Gene SWISSPROT- ID:P08514 PLATELET MEMBRANE GLYCOPROTEIN IIB PRECURSOR (GPIIB) (INTEGRIN ALPHA- IIB) (CD41) - HOMO SAPIENS (HUMAN), 1039 aa.
ATPase_as sociated	biotindep	cadherin
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
(711)	Ser (712)	Ala (713)
Thr	O O	Pro
⊢		9
O	U	O
TGTATTCCTGTAA TGGGGCTGATGA[C/TJATATATGATG GTTATGGACCACC AC	GCCCCTGAGCAG TCAGGACCCGGC T[C/T]CCGTCCGT GAGTGCCACGAT CCCAG	GGAGTGGGTGCT GCTGCTTGGG A[C/G]CTTGTGCT GCCCTCCAGCC TGGGC
	929	267
cg43252813 2306	cg43920913	cg40310734
482	483	484

17 (17q21.3 2)	1 (1923)
0	1.00E-218 1 (1q23)
Human Gene SWISSPROT- ID:P08514 PLATELET MEMBRANE GLYCOPROTEIN IIB PRECURSOR (GPIIB) (INTEGRIN ALPHA- IIB) (CD41) - HOMO SAPIENS (HUMAN), 1039 aa.	Human Gene SWISSPROT- ID:P14151 L-SELECTIN PRECURSOR (LYMPH NODE HOMING RECEPTOR) (LEUKOCYTE ADHESION MOLECULE-1) (LAM-1) (LEUKOCYTE SURFACE ANTIGEN LEU-8) (TQ1) (GP90-MEL) (LEUKOCYTE-ENDOTHELIAL CELL ADHESION MOLECULE 1) (LECAM1) (CD62L) - HOMO SAPIENS (HUMAN), 372 aa.
cadherin	cadherin
NON- CONSER VATIVE	NON- CONSER VATIVE
Ala (714)	Leu (715)
Pro	Phe
<u>o</u>	O
O	H-
CGTGTCCTCCCTC C CCCTATGCGGTG[C/G]CCCGCTCA GCCTGCCCCGAG GCGA	GGGGTACTATGG GCCCCAGTGTCA G[T/C]TTGTGATTC AGTGTGAGCCTTT GGA
3111	7777
cg40310734 3111	cg43956560
485	486

1 (1923)	4	
1.00E-218 1 (1q23)	7.00E-172 4	0
Human Gene SWISSPROT- ID:P14151 L-SELECTIN PRECURSOR (LYMPH NODE HOMING RECEPTOR) (LEUKOCYTE ADHESION MOLECULE-1) (LAM-1) (LEUKOCYTE SURFACE ANTIGEN LEU-8) (TQ1) (GP90-MEL) (LEUKOCYTE-ENDOTHELIAL CELL ADHESION MOLECULE 1) (LECAM1) (CD62L) - HOMO SAPIENS (HUMAN), 372 aa.	Human Gene SWISSPROT- ID:P21815 BONE SIALOPROTEIN II PRECURSOR (BSP II) (CELL- BINDING SIALOPROTEIN) (INTEGRIN-BINDING SIALOPROTEIN) - HOMO SAPIENS (HUMAN), 317 aa.	calcium_cha_Human Gene SWISSPROT-ID:P21817 RYANODINE RECEPTOR, SKELETAL MUSCLE (SKELETAL MUSCLE CALCIUM RELEASE CHANNEL) - HOMO SAPIENS (HUMAN), 5032 aa.
cadherin	cadherin	calcium_cha nnel
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Ser (716)	Gly (717)	Cys (718)
O O	Arg	Arg
⊢	o O	 -
U	∢	O
GCTGGGTACCAT GGACTGTACTCAC [C/T]CTTTGGGAAA CTTCAGCTTCAGC TC	TGCAGAAGGCAC CACAGAGACCGG A[A/G]GGCAGGGC AAGGGCACCTCG AAGAC	GTGTGTGTGTAAT GGTGTGGCTGTA C/TIGCTCCAACCA AGATCTTATTACT GA
	753	1945
cg43956560 837	cg42388009	cg43977436
487	488	489

			X (Xq22)
7	9	ဖ	×
C	0	0	0
carboxylase Human Gene SWISSPROT- ID:P38435 VITAMIN K-DEPENDENT GAMMA-CARBOXYLASE (EC 6.4) (GAMMA-GLUTAMYL CARBOXYLASE) - HOMO SAPIENS (HUMAN), 758 aa.	HA 1(X)	Human Gene SWISSPROT- ID:Q03692 COLLAGEN ALPHA 1(X) CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 680 aa.	Human Gene SPTREMBL-ID:Q12823 A TYPE IV COLLAGEN - HOMO SAPIENS (HUMAN), 1690 aa (fragment).
carboxylase	collagen	collagen	collagen
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Arg (719)	Gly (720)	Met (721)	Thr (722)
u U	qu	TH.	<u>ə</u>
<u>ه</u>	ပ	 -	ပ
⋖	A	O	A
CGGAAGCTGGTG A TCCTACTGCCCCC [A/G]AAGGTTGCA ACAACTGTTGCCC CTC	CCAGGGCCTCCA GGTCCAAGAGGC C[A/C]CTCTGGAG AGCCTGGTCTTCC AGGG	GTGTTTTACGCTG C AACGATACCAAA[C/TJGCCCACAGG CATAAAAGGCCCA	TCCAGGAATACCA A GGTCTGCCTGGT[A/G]TTCCTGGAAC AAGAGGATTAAAA GG
1130	1595	176	2855
cg43280376 1130	cg42201364	cg42201364 176	cg40339378
490	491	492	493

1 (1p32)	1 (1p32)	5 (5p13)	1 (1p21)
0	0	0	5.00E-304
complement Human Gene SWISSNEW- ID:P07358 COMPLEMENT COMPONENT C8 BETA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 591 aa.lpcis:SWISSPROT-ID:P07358 COMPLEMENT COMPONENT C8 BETA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 591 aa.	complement Human Gene SWISSPROT-ID:P07357 COMPLEMENT COMPONENT C8 ALPHA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 584 aa.	complement Human Gene TREMBLNEW-ID:G386348 COMPLEMENT C6 - HOMO SAPIENS, 941 aa.	Human Gene SWISSPROT- ID:P09603 MACROPHAGE COLONY STIMULATING FACTOR-1 PRECURSOR (CSF-1) (MCSF) - HOMO SAPIENS (HUMAN), 554 aa.
complement	complement	complement	csf
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Gly (723)	Gln (724)	Ala (725)	Pro (726)
Arg	Lys	Olu Glu	ren
O	ပ	U	O
<	⋖	4	-
AGACTGTGTTACC A AACAGACCATGCI AGIGAAGTCAAGT GCGATGTGAAGG CTT	CTCCAGTTCTACA A ACTGTGTAAGG[ACJAAGCACAGTG TGGACAGGATTTC CA	CAGTTTGGGGGA CAGCCATGCACT G[A/C]GCCTCTGG TAGCCTTTCAACC ATGC	CCAGGCTCTCCC AGGATCTCATCAC [T/C]GCGCCCCCA GGGCCTCAGCAA CCCC
909		533	1347
cg43063256	cg44032748 414	cg43049885	cg21644442
494	495	496	497

ი	17
	1.70E-52
Human Gene Similar to SWISSNEW- 1.10E-77 ID:P08700 INTERLEUKIN-3 PRECURSOR (IL-3) (MULTIPOTENTIAL COLONY-STIMULATING FACTOR) (HEMATOPOIETIC GROWTH FACTOR) (MCGF) - HOMO SAPIENS (HUMAN), 152 aa.jpcls:SWISSPROT-ID:P08700 INTERLEUKIN-3 PRECURSOR (IL-3) (MULTIPOTENTIAL COLONY-STIMULATING FACTOR) (HEMATOPOIETIC GROWTH FACTOR) (P-CELL STIMULATING FACTOR) (MAST-CELL GROWTH FACTOR) (MGGF) - HOMO SAPIENS (HUMAN), 152 aa.	Human Gene Similar to SWISSPROT-ID:P21592 CYTOCHROME C OXIDASE ASSEMBLY PROTEIN COX10 PRECURSOR - SACCHAROMYCES CEREVISIAE (BAKER'S YEAST), 462 aa.
csf	cytochrome
NON- CONSER VATIVE	NON- CONSER VATIVE
Ser (727)	His (728)
P 70	Tyr
-	O .
O	4
CCAAGCTCCCATG C ACCCAGACAG[C/I]CCTTGAAGAC AAGCTGGGTTAAC TG	TCCACGTAGAAGC A GGAAGCCGAGGT[A/GJGGAGATGTAC GCATTGATGGGAA GG
279	1651
cg2753430	cg43923204
88 8	499

22	1 (1p36.2)	4 (4q22)
	8.80E-78	1.30E-209
cytochrome Human Gene Similar to SPTREMBL- 2.40E-52 ID:000761 CYTOCHROME OXIDASE SUBUNIT VIA HEART ISOFORM PRECURSOR (EC 1.9.3.1) (CYTOCHROME-C OXIDASE) (CYTOCHROME A(3)) (CYTOCHROME AA(3)) - HOMO SAPIENS (HUMAN), 97 aa.	Human Gene Similar to SWISSPROT-ID:P32320 CYTIDINE DEAMINASE (EC 3.5.4.5) (CYTIDINE AMINOHYDROLASE) - HOMO SAPIENS (HUMAN), 146 aa. [pcls: TREMBLNEW-ID:E1228801 CYTIDINE DEAMINASE (EC 3.5.4.5) - HOMO SAPIENS (HUMAN), 146 aa.	dehydrogen Human Gene SWISSNEW- ase ID:P08319 ALCOHOL DEHYDROGENASE CLASS II PI CHAIN (EC 1.1.1.1) - HOMO SAPIENS (HUMAN), 391 aa. pcls:SWISSPROT-ID:P08319 ALCOHOL DEHYDROGENASE CLASS II PI CHAIN (EC 1.1.1.1) - HOMO SAPIENS (HUMAN), 391 aa.
cytochrome	deaminase	dehydrogen ase
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Gin (729)	Gin (730)	Gly (731)
<u>ଟ</u> ତ	Lys	End
 -	U	O
O	<	F
TTGGTAGGGACG GAACTCGGGGCG C[G/T]GGCGGTGG CCCGAGTGGAGA TAGGA	GCTGGTTTGCTCC A CAGGAGGCCAAG[ACJAGTCAGCCTA CTGCCCCTACAGT CA	AAGCATCCGAACA ATCCTCATCTTT[1/ GJGAAGATGCCAG GAGCAATTCGGAA T
174	279	1618
cg44017721 174	cg41626024	cg43057018
500	501	502

		1p36.13
3.90E-86 1	.50E-57 1	
dna_rna_bi Human Gene Similar to nd TREMBLNEW-ID:G913312 DNA BINDING PROTEIN MEF2 {CLONE XMEF2A1} - XENOPUS LAEVIS, 516 aa.		Human Gene Similar to SWISSNEW- 1.30E-60 ID:Q02535 DNA-BINDING PROTEIN INHIBITOR ID-3 (ID-LIKE PROTEIN INHIBITOR HLH 1R21) (HELIX-LOOP-HELIX PROTEIN HEIR-1) - HOMO SAPIENS (HUMAN), 119 aa. pcls:SWISSPROT-ID:Q02535 DNA-BINDING PROTEIN INHIBITOR ID-3 (ID-LIKE PROTEIN INHIBITOR HLH 1R21) (HELIX-LOOP-HELIX PROTEIN HEIR-1) - HOMO SAPIENS (HUMAN), 119 aa.
dna_rna_bi nd	dna_ma_bi nd	dna_rna_bi nd_inhib
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Ala (732)	Lys (733)	Thr (734)
Thr	Asn	Ala
O	⋖	
4	U	O
CCGCACCAACGC A CGACATCATCGAG [A/G]CCCTGAGGA AGAGGGCTTCAA GGG	TCCACGACCGGG TAGAGAACTACAA [C/A]CCGCGGCAG CGCAAGCTCCGC	TCGTTGGAGATGA CAAGTTCCGGAGI C/TJGAGCTCGGCT GTCTGGATGGGA AGG
	2205	707
cg42837709 464	cg43327954	cg43971258 707
503	504	505

3)	
11 (11q23)	
1.80E-203 11 (11q ²	1.90E-178
Human Gene SWISSNEW- ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa. pdis:SWISSPROT-ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa.	Human Gene SWISSNEW- ID:Q15166 SERUM PARAOXONASE/ARYLESTERASE 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) (SERUM ARYLDIAKYLPHOSPHATASE 3) (A- ESTERASE 3) - HOMO SAPIENS (HUMAN), 341 aa (fragment). pcls:SWISSPROT- ID:Q15166 SERUM PARAOXONASE/ARYLESTERASE 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) (SERUM ARYLDIAKYLPHOSPHATASE 3) (A- ESTERASE 3) - HOMO SAPIENS (HUMAN), 341 aa (fragment).
u de	esterase
NON- CONSER VATIVE	NON- CONSER VATIVE
His (735)	(736) (736)
<u>ต</u>	<u>G</u>
	—
<u>ග</u>	U
AGCTGGAGCAAC AGCAGGAACAGC A[G/T]CAGGAGCA GCAGCAGGAGCA GGTGC	GTTTGGCATACCT GGATATTTTAAT[C MJCAGTGGAGATA AAAGACAGCCCA CT
1253	1063
cg41554010	cg43957743
506	202

	15 (15q15)
1.90E-178	9.30E-106
Human Gene SWISSNEW- ID:Q15166 SERUM PARAOXONASE/ARYLESTERASE 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) (SERUM ARYLDIAKYLPHOSPHATASE 3) (A- ESTERASE 3) - HOMO SAPIENS (HUMAN), 341 aa (fragment), Ipcls:SWISSPROT- ID:Q15166 SERUM PARAOXONASE/ARYLESTERASE 3 (EC 3.1.1.2) (EC 3.1.8.1) (PON 3) (SERUM ARYLDIAKYLPHOSPHATASE 3) (A- ESTERASE 3) - HOMO SAPIENS (HUMAN), 341 aa (fragment).	Human Gene Homologous to SWISSPROT-ID:P21781 KERATINOCYTE GROWTH FACTOR PRECURSOR (KGF) (FIBROBLAST GROWTH FACTOR- 7) (FGF-7) (HBGF-7) - HOMO SAPIENS (HUMAN), 194 aa.
esterase	fgf
NON- CONSER VATIVE	NON- CONSER VATIVE
Ala (737)	Glu (738)
Je S	Lys
ن د	ပ
4	⋖
TATTTTAATCCAG TGGAGATAAAAG[A/CJCAGCCCACTA GGAAGTATATCAA TA	AAGTGAATTCTAT ACTTGCAATGAACLAGJAGGAAGGAAAAACTCTATGCAAAGAAAAAAAAAAAAA
1079	812
cg43957743	cg43248101
208	509

	7
7.40E-80	0
glucuronida Human Gene Similar to SWISSPROT-ID:P08236 BETA- GLUCURONIDASE PRECURSOR (EC 3.2.1.31) (BETA-G1) - HOMO SAPIENS (HUMAN), 651 aa.	glycoprotein Human Gene SWISSNEW- ID:P40967 MELANOCYTE PROTEIN PMEL 17 PRECURSOR (MELANOCYTE LINEAGE- SPECIFIC ANTIGEN GP100) (MELANOMA-ASSOCIATED ME20 ANTIGEN) (ME20M/ME20S) (ME20- M/ME20-S) (95 KD MELANOCYTE- SPECIFIC SECRETED GLYCOPROTEIN) - HOMO SAPIENS (HUMAN), 661 aa. pcls:SWISSPROT-ID:P40967 MELANOCYTE PROTEIN PMEL 17 PRECURSOR (MELANOCYTE LINEAGE-SPECIFIC ANTIGEN GP100) (MELANOMA-ASSOCIATED ME20-S) (95 KD MELANOCYTE- SPECIFIC SECRETED GLYCOPROTEIN) - HOMO SAPIENS (HUMAN), 661 aa.
glucuronida se	glycoproteir
NON- CONSER VATIVE	CONSER VATIVE
1le (739)	(740)
Arg	G 5
4	O
U	O .
GATGAGCTCTCCA C ACCACGTATTT[C /AJTGCGTTTTTGA TCCAGACCCAGAT G	CACCAGCAAGAT GCCCACGATCAG CGAGGCCTGCT CCAAGGCCTGCTT CTTG
332	387
cg43969014 332	cg43286488
510	211

0	0	0
glycoprotein Human Gene SWISSPROT- ID:Q12889 OVIDUCT-SPECIFIC GLYCOPROTEIN PRECURSOR (OVIDUCTAL GLYCOPROTEIN) (OVIDUCTIN) (ESTROGEN- DEPENDENT OVIDUCT PROTEIN) - HOMO SAPIENS (HUMAN), 678 aa.	glycoprotein Human Gene SWISSPROT- ID:Q12889 OVIDUCT-SPECIFIC GLYCOPROTEIN PRECURSOR (OVIDUCTAL GLYCOPROTEIN) (OVIDUCTIN) (ESTROGEN- DEPENDENT OVIDUCT PROTEIN) - HOMO SAPIENS (HUMAN), 678 aa.	glycoprotein Human Gene SWISSPROT- ID:Q12889 OVIDUCT-SPECIFIC GLYCOPROTEIN PRECURSOR (OVIDUCTAL GLYCOPROTEIN) (OVIDUCTIN) (ESTROGEN- DEPENDENT OVIDUCT PROTEIN) - HOMO SAPIENS (HUMAN), 678 aa.
glycoprotein	glycoprotein	glycoprotein
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
His (741)	Pro (742)	Thr (743)
Tyr	Ser	Met
O	O	O
A	A	∢
TTTTCCCCAGGGG A TCACAGACTGAT[A/GJACCCACAGAG GTCAGGGTCTTCT GT	GGGGTCACAGAC A TGATAACCCACAG [A/G]GGTCAGGGT CTTCTGTCCAGTG GTC	CTGATGACCCACA A GAAGTCATGGTC[A/G]TTGCCCCAGT GATCTCAGTCTTC TC
663	672	773
cg44004239 663	cg44004239	cg44004239 773
512	513	514

(11pter)	1 (1921)
1.80E-195	2.00E-183 1 (1q21)
glycoprotein Human Gene SWISSPROT- ID:P16070 CD44 ANTIGEN PRECURSOR (PHAGOCYTIC GLYCOPROTEIN I) (PGP-1) (HUTCH-I) (EXTRACELLULAR MATRIX RECEPTOR-III) (ECMR-III) (GP90 LYMPHOCYTE HOMING/ADHESION RECEPTOR) (HERMES ANTIGEN) (HEPARAN SULFATE PROTEOGLYCAN) (EPICAN) (CDW44) - HOMO SAPIENS (HUMAN), 742 aa.	Human Gene SWISSNEW- ID:P06126 T-CELL SURFACE GLYCOPROTEIN CD1A PRECURSOR (CD1A ANTIGEN) (T-CELL SURFACE ANTIGEN T6/LEU-6) (HTA1 THYMOCYTE ANTIGEN) - HOMO SAPIENS (HUMAN), 327 aa.jpcls:SWISSPROT-ID:P06126 T-CELL SURFACE GLYCOPROTEIN CD1A PRECURSOR (CD1A ANTIGEN) (T-CELL SURFACE ANTIGEN T6/LEU-6) (HTA1 THYMOCYTE ANTIGEN) - HOMO SAPIENS (HUMAN), 327 aa.
	glycoprotein
NON- CONSER VATIVE	NON- CONSER VATIVE
Tyr (744)	(745)
Ser	년 H
<u> </u>	<u> </u>
ATATGTGTCATAC G TGGGAGGTGTTG[G/IJATGTGAGGAT GTACACCCCTGTG TT	AAGGAGCCTCTCT C CCTTCCATGTCA[C/I)CTGGATCGCA TCCTTTTACAACC AT
	622
cg43932434 1504	cg40915005
515	5 9

-		
1 (192)		
2.00E-183 1 (1q21)	6.40E-91	6.40E-91
2.00	6.4(6.4
glycoprotein Human Gene SWISSNEW- ID:P06126 T-CELL SURFACE GLYCOPROTEIN CD1A PRECURSOR (CD1A ANTIGEN) (T-CELL SURFACE ANTIGEN T6/LEU-6) (HTA1 THYMOCYTE ANTIGEN) -HOMO SAPIENS (HUMAN), 327 aa. pcls:SWISSPROT-ID:P06126 T-CELL SURFACE GLYCOPROTEIN CD1A PRECURSOR (CD1A ANTIGEN) (T-CELL SURFACE ANTIGEN T6/LEU-6) (HTA1 THYMOCYTE ANTIGEN) - HOMO SAPIENS (HUMAN), 327 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P38159 HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN G (HNRNP G) (GLYCOPROTEIN P43) - HOMO SAPIENS (HUMAN), 437 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P38159 HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN G (HNRNP G) (GLYCOPROTEIN P43) - HOMO SAPIENS (HUMAN), 437 aa.
glycoprotein	glycoprotein	glycoprotein
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Cys (746)	Cys (747)	Thr (748)
d L	Tyr	Lys
O	O	ပ
ပ	4	4
ATTCCAGCACCAT G CGTTTTCCTGTG[G/CJCCCTGGTCCA GGGGAAACTTCA GCA	GTGCTCCCTGATC A CTCGTGAAGCAT[A/G]TGGTAGCTCA AGTTATGTGGCAT CT	AATGCTGCGAAAG A ATATGAATGGAA[A /C]GTCTTTGCATG GAAAGCAATAAA A
737	1529	329
cg40915005	cg36834323	cg36834323
517	518	519

	1		2
6.40E-91	2.50E-80	9.40E-58	2.60E-188 2
glycoprotein Human Gene Similar to SWISSPROT-ID:P38159 HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN G (HNRNP G) (GLYCOPROTEIN P43) - HOMO SAPIENS (HUMAN), 437 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:P04216 THY-1 MEMBRANE GLYCOPROTEIN PRECURSOR (THY-1 ANTIGEN) (CDW90) (CD90 ANTIGEN) - HOMO SAPIENS (HUMAN), 161 aa.	glycoprotein Human Gene Similar to SWISSPROT-ID:Q05910 CELL SURFACE ANTIGEN MS2 PRECURSOR (EC 3.4.24) (MACROPHAGE CYSTEINE- RICH GLYCOPROTEIN) (CD156 ANTIGEN) - MUS MUSCULUS (MOUSE), 826 aa.	Human Gene SWISSPROT-ID:P28356 HOMEOBOX PROTEIN HOX-D9 (HOX-4C) (HOX-5.2) -HOMO SAPIENS (HUMAN), 342 aa.
glycoprotein	glycoprotein	glycoprotein	homeobox
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Arg (749)	His (750)	Gly (751)	Asp (752)
Ser	Asn	Arg	Ala
O	O	O	—
⋖	F	4	ග
AAGTCTGAGATCT A GCAAGAGGAAGC[AVCJGTGGAGGAA CAAGAGGGTGGC TTCC	GCGGATAAGTAG AGGACCTTCATGT [T/G]GTATTTGCTG GTGAAGTTGGTTC GG	CTTAGACATACAA TATACTTACCTT[A/ GJGAGGTCACGTA TGTTTGTCCGCAC A	GGAGCGAGCGTG GATCCAGTTCGC GGATJCGGGGTTG TTTGGGTCAAGTT GCTG
463	1697	1665	086
cg36834323	cg44019290	cg42336656	cg42730678
520	521	522	523

	2 (2q21)	-
1.10E-123	0	0
	Human Gene SWISSPROT- ID:P09848 LACTASE-PHLORIZIN HYDROLASE PRECURSOR (EC 3.2.1.108) (EC 3.2.1.62) (LACTASE- GLYCOSYLCERAMIDASE) - HOMO SAPIENS (HUMAN), 1927 aa.	Human Gene SWISSPROT- ID:Q16666 GAMMA-INTERFERON- INDUCIBLE PROTEIN IFI-16 (INTERFERON-INDUCIBLE MYELOID DIFFERENTIATION TRANSCRIPTIONAL ACTIVATOR) - HOMO SAPIENS (HUMAN), 729 aa. [pcls:SPTREMBL-ID:Q16666 IF116=INTERFERON-INDUCIBLE MYELOID DIFFERENTIATION TRANSCRIPTIONAL ACTIVATOR - HOMO SAPIENS (HUMAN), 729 aa (fragment).
homeobox	hydrolase	interferon
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Ser (753)	Ala (754)	His (755)
<u>=</u>	Thr	Asp
ග	O	ڻ ن
<u> </u>	4	O
GCCCTGTGCCTG ACGGAGAGGCAG A[T/G]CAGGATATG GTTCCAGAACCGA CGC	CTGGGCACCATAT AGGATAGCCCAC A/G)CCGTCATCAA AGCCCATGCCAG AGT	GTGGAGGGTGCA GGTGAAGTAGCAT [C/G]CACTTCCTTC TTCCTCTTTTTTG AT
769	3297	2172
cg42714160	cg42359655	cg43925670 2172
524	525	526

10	21 (21q22.1)	14 (14q32.3)	11 (20p13)	11 (20p13)
		1.40E-262	2.00E-215	2.00E-215
Human Gene SWISSPROT- ID:Q04759 PROTEIN KINASE C, THETA TYPE (EC 2.7.1) (NPKC- THETA) - HOMO SAPIENS (HUMAN), 706 aa.	Human Gene SWISSPROT- ID:Q13627 SERINE/THREONINE- SPECIFIC PROTEIN KINASE MINIBRAIN HOMOLOG (EC 2.7.1) (HP86) (DYRK) - HOMO SAPIENS (HUMAN), 763 aa.	Human Gene SWISSPROT- ID:P31749 RAC-ALPHA SERINE/THREONINE KINASE (EC 2.7.1) (RAC-PK-ALPHA) (PROTEIN KINASE B) (PKB) (C-AKT) - HOMO SAPIENS (HUMAN), 480 aa.	Human Gene SWISSPROT- ID:P19138 CASEIN KINASE II, ALPHA CHAIN (CK II) (EC 2.7.1.37) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 391 aa.	Human Gene SWISSPROT- ID:P19138 CASEIN KINASE II, ALPHA CHAIN (CK II) (EC 2.7.1.37) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 391 aa.
kinase	kinase	kinase	kinase	kinase
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Leu (756)	Asn (757)	Ser (758)	Val (759)	Arg (760)
Pro	Lys	Gly	Met	Ser
<u> </u>	 -	F	U	O
O	₀	O	F	 -
TGCTCCATCAAAA ATGAAGCAAGGCI C/TJGCCATGTTTA CCGACACCGGGA	CAAAAGCAAGAAA GTTCTTTGAGAA[GAJTTGCCAGATG GCACTTGGAACTT AA	AGTCCACCGCCG CCTCAGGCCGTG C[C/T]GCTGGCCG AGTAGGAGAACT GGGGG	GGCACTGAAGAA ATCCCTGACATCA [T/C]ATTGGCGCT GCTGACGGGCGT ACTG	GGGCTGACAAGG TGCTGATTITCACI T/GJGTGGACAAAG CGTTCCCATCGCT TT
1083	2663	1226	1429	1621
cg43090990	cg43969763	cg43932396	cg43917871	cg43917871
527	528	529	530	531

(20p13)	11 (20p13)	19 (19q13.1)
2.00E-215 11 (20p1	2.00E-215 11 (20	
Human Gene SWISSPROT- ID:P19138 CASEIN KINASE II, ALPHA CHAIN (CK II) (EC 2.7.1.37) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 391 aa.	Human Gene SWISSPROT- ID:P19138 CASEIN KINASE II, ALPHA CHAIN (CK II) (EC 2.7.1.37) - HOMO SAPIENS (HUMAN), AND BOS TAURUS (BOVINE), 391 aa.	kinaserecep Human Gene SWISSNEW- ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.jpcls:SWISSPROT-ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.
Kinase	kinase	kinaserecep tor
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER tor VATIVE
Gly (761)	Phe (762)	(763)
Asp	ren	Th.
U	O	O
H	F-	4
TTCAATGTTGTAT TTGTCAATATAG[T /C]CATATAAATCTT CTGTCCCCAGAAC	TGTAAAATCGAAT ATCATAGTCTGTIT /GJAACGTCTGGTA CAATTGCTTGAAG	TCGGCTAGGCAG CCTCCATCCTCAC [A/C]CCCCTTATCA CATCGCGTGGC ATG
1713	2096	1107
cg43917871 1713	cg43917871 2096	cg43322545
532	533	534

(19q13.1)
o
kinaserecep Human Gene SWISSNEW- ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa. pcls:SWISSPROT-ID:P30530 TYROSINE-PROTEIN KINASE RECEPTOR UFO PRECURSOR (EC 2.7.1.112) (AXL ONCOGENE) - HOMO SAPIENS (HUMAN), 887 aa.
kinaserecep tor
NON- CONSER for VATIVE
Gly (764)
Asp
<u>o</u>
A
TTCCTCCTCTATT A CCCGGCTCGGGG [A/G]CCAGCCAGT GTACCTGCCCACT CAG
2116
cg43322545 2116
535

(14q21)	6 (6p21.3)
3.50E-138	9.10E-147
Human Gene Homologous to SWISSNEW-ID:P17931 GALECTIN-3 (GALACTOSE-SPECIFIC LECTIN 3) (MAC-2 ANTIGEN) (IGE-BINDING PROTEIN) (35 KD LECTIN) (CARBOHYDRATE BINDING PROTEIN) (BINDING PROTEIN) (LECTIN L-29) (L-31) (GALACTOSIDE-BINDING PROTEIN) (GALBP) - HOMO SAPIENS (HUMAN), 249 aa. Ipcls:SWISSPROT-ID:P17931 GALECTIN-3 (GALACTOSE-SPECIFIC LECTIN 3) (MAC-2 ANTIGEN) (IGE-BINDING PROTEIN) (35 KD LECTIN) (CARBOHYDRATE BINDING PROTEIN) (GALACTOSIDE-BINDING PROTEIN) (GALACTOSIDE-BINDING PROTEIN) (GALACTOSIDE-BINDING PROTEIN) (GALACTOSIDE-BINDING PROTEIN) (SAPIENS (HUMAN), 249 aa.	Human Gene Homologous to SWISSPROT-ID:P28068 CLASS II HISTOCOMPATIBILITY ANTIGEN, M BETA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 263 aa.
a mining	MHC
NON- CONSER VATIVE	NON- CONSER VATIVE
His (765)	Glu (766)
٥ 2	Ala
<u> </u>	A
O	O
TCCGGGATAAGCT CCAGGTGCTCCA G/TJGGTAGGCGC CTGGAGGTGCCT GTCC	AAGCTTGTCATGC CTCACAGCAGTG[C/A]GCACAAGACT GCCCAGCCCAAT GGA
8 0 3	718
cg43958558	cg43966144
536 2	537

6 (6p21.3)	6 (6p21.3)	19	19	~
9.10E-147	3.70E-134	1.80E-113	1.80E-113 19	2.30E-71
Human Gene Homologous to SWISSPROT-ID:P28068 CLASS II HISTOCOMPATIBILITY ANTIGEN, M BETA CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 263 aa.	Human Gene Homologous to SWISSPROT-ID:P06340 HLA CLASS II HISTOCOMPATIBILITY ANTIGEN, DZ ALPHA CHAIN PRECURSOR (MHC DN-ALPHA) - HOMO SAPIENS (HUMAN), 250 aa.	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	Human Gene Homologous to SPTREMBL-ID:Q95368 HLA CLASS I INHIBITORY NK RECEPTOR - HOMO SAPIENS (HUMAN), 455 aa.	misc_chann Human Gene Similar to SPTREMBL- 2.30E-71 ID:P91197 SIMILAR TO LIGAND- GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.
MHC	МНС	MHC	MHC	misc_chann el
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Thr (767)	lle (768)	Ala (769)	Ala (770)	Ala (771)
<u>e</u>	rd T	Pro	Th.	Thr
O	- -	ပ	O	_O
-	O	O	∢	A
ACTTACACCTGTG TGGTAGAGCACA[T/CJTGGGGCTCCT GAGCCCATCCTTC GG	GGCCTGGTGGGC TTCCTCGTGGGCA [C/T]CGTCCTCATC ATCATGGGCACAT AT	CTGAGCCCAGAG CGTTGTCTCCTGC [C/G]CATGAGCAC CACAGTCAGGCC TTGA	AGCCGGCCGGG CCCCACGGTTCG C[A/G]CAGGAGAG AACGTGACCTTGT CCTG	CCGGCTGTGCTC AGGGGTGTGGGG T[A/G]CGGATACA GAGGAGCGGCTG GTGGA
823	206	1044	424	340
cg43966144 823	cg42686658	cg38337333	cg38337333	cg42481172
538	539	540	541	542

8 (8p11.2)	8 (8p11.2)	17 (17q11.2)	X (Xq11)	
	6.10E-70	0	0	1.40E-157
misc_chann Human Gene Similar to SPTREMBL- 6.10E-70 ID:P91197 SIMILAR TO LIGAND-GATED IONIC CHANNEL PROTEIN - CAENORHABDITIS ELEGANS, 461 aa.	REMBL- AND- ROTEIN ANS,	Human Gene SWISSPROT- ID:P20393 V-ERBA RELATED PROTEIN EAR-1 - HOMO SAPIENS (HUMAN), 614 aa.	Human Gene SWISSNEW- ID:P10275 ANDROGEN RECEPTOR - HOMO SAPIENS (HUMAN), 919 aa.lpcls:SWISSPROT-ID:P10275 ANDROGEN RECEPTOR - HOMO SAPIENS (HUMAN), 919 aa.	Human Gene TREMBLNEW-ID:G2935442 RIBONUCLEASE H1 - HOMO SAPIENS (HUMAN), 286 aa.jpcls:TREMBLNEW-ID:G2935444 RIBONUCLEASE H1 - HOMO SAPIENS (HUMAN), 286 aa.
misc_chann el	misc_chann el	nucl_recpt	nucl_recpt	nuclease
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Leu (772)	Gln (773)	Leu (774)	His (775)	Phe (776)
Тгр	Lys	His	ug U	Leu
<u> </u>	O	F	U	F
ව	⋖	A	O	U
GAAGATGCCCTC CTCAGACATGAGT [G/T]GAAAGGTTAT CAGAAATGGGTC CGC	AGACATGAGTGG AGACATGAGTGG ACJAAGGTTATCA GAAATGGGTCCG CCC	GCCTCGGGCTTC CACTACGGTGTG C[A/T]CGCCTGCG AGGGCTGCAAGG	AGCGGGACGGTC CGGAGCAAGCCC A[G/C]AGGCAGAG GAGGCGACAGAG GGAAA	GTGCCGGGAGTG AGCGATGAGCTG G[C/I]TTCTGTTCC TGGCCACAGAG
238	240	1067	89	91
cg3000465	cg3000465	cg43249083	cg44928796	cg43323772
543	544	545	546	547

			14 14q24.1
	12	12	· • · · · · · · · · · · · · · · · · · ·
	1.10E-97	1.10E-97	8.90E-101
Human Gene Homologous to SPTREMBL-ID:Q13692 BCR/ABL FUSION PROTEIN - HOMO SAPIENS (HUMAN), 284 aa (fragment).	Human Gene Similar to SWISSPROT-ID:P01118 TRANSFORMING PROTEIN P21/K- RAS 2B - HOMO SAPIENS (HUMAN), 188 aa.	Human Gene Similar to SWISSPROT-ID:P01118 TRANSFORMING PROTEIN P21/K- RAS 2B - HOMO SAPIENS (HUMAN), 188 aa.	Human Gene Homologous to SWISSPROT-ID:P18283 GLUTATHIONE PEROXIDASE- GASTROINTESTINAL (EC 1.11.19) (GSHPX-GI) (GLUTATHIONE PEROXIDASE-RELATED PROTEIN 2) (GPRP) - HOMO SAPIENS (HUMAN), 190 aa.
oncogene	oncogene	оисодепе	peroxidase
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Phe (777)	Cys (778)	His (779)	Ser (780)
Cys	Gly	GIN	Cys
<u> </u>	F	U	F
GGCTATAATCACA G ATGGGGAATGGT[G/TJTGAAGCCCAA ACCAAAAATGGCC	ATATAAACTTGTG G GTAGTTGGAGCT[G/TJGTGGCGTAG GCAAGAGTGCCTT GAC	TGGATATTCTCGA A CACAGCAGGTCA[A/C]GAGGAGTACA GTGCAATGAGGG	CTGTTCAGGATCT A CCTCATTCTGAC[A TJGTTCTCCTGAT GTCCAAATTGGTT G
808	155	304	206
cg42732993	cg42904626	cg42904626	cg42691989
548	549	250	551
	-		

_		11 (11q22)	
0	0	3.20E-302	2.40E-155
/- OR-LIKE SOR - , 1015	Human Gene SWISSPROT- ID:P23469 PROTEIN-TYROSINE PHOSPHATASE EPSILON PRECURSOR (EC 3.1.3.48) (R-PTP-EPSILON) - HOMO SAPIENS (HUMAN), 700 aa.	phosphatas Human Gene SWISSPROT- ID:P54613 PROTEIN PHOSPHATASE PP2A, 65 KD REGULATORY SUBUNIT, BETA ISOFORM (PROTEIN PHOSPHATASE PP2A SUBUNIT A, BETA ISOFORM) (P65-BETA) - SUS SCROFA (PIG), 602 aa (fragment).	phosphoryla Human Gene SWISSPROT- se ID:P00491 PURINE NUCLEOSIDE PHOSPHORYLASE (EC 2.4.2.1) (INOSINE PHOSPHORYLASE) (PNP) - HOMO SAPIENS (HUMAN), 289 aa.
phosphatas e	phosphatas e	phosphatas e	phosphoryla se
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Pro (781)	Glu (782)	Thr (783)	Ser (784)
Ser	Gly	<u>•</u>	Qi y
<u>o</u>	H	O	F
⋖	O	∢	U
AGGTCCTCGCGG AGCTGGGTCCGG G[A/G]CCCGGGAG GGTAGGTCAGCG CAGAC	CTGGCGCACTACT CGGACCTGCTCC C/TCCTGGCGGG CCTGGGGCTGAT TGAG	GCACAAGGAACG GAATTGCTGTCTG [A/G]TTCTGCTTT AACAGCATTTGAT GC	CTTCGGGGAAAG TTGGGGATTTCAC [C/T]GTAGTCAAAG ATCTGGGCCTGA GTT
4096	368	3187	1330
cg43917453	cg43947363	cg43928335	cg43996195
552	553	554	555

(19q13.3)	6 (6p12)
	0
polymerase Human Gene SWISSNEW- ID:P28340 DNA POLYMERASE DELTA CATALYTIC CHAIN (EC 2.7.7.7) - HOMO SAPIENS (HUMAN), 1107 aa. pcls:SWISSPROT-ID:P28340 DNA POLYMERASE DELTA CATALYTIC CHAIN (EC 2.7.7.7) - HOMO SAPIENS (HUMAN), 1107 aa.	Human Gene SWISSNEW- ID:P25205 DNA REPLICATION LICENSING FACTOR MCM3 (DNA POLYMERASE ALPHA HOLOENZYME-ASSOCIATED PROTEIN P1) (RLF BETA SUBUNIT) (P102 PROTEIN) - HOMO SAPIENS (HUMAN), 808 aa.jpcls:SWISSPROT-ID:P25205 DNA REPLICATION LICENSING FACTOR MCM3 (DNA POLYMERASE ALPHA HOLOENZYME-ASSOCIATED PROTEIN P1) (RLF BETA SUBUNIT) (P102 PROTEIN) - HOMO SAPIENS (HUMAN), 808 aa.
polymerase	polymerase
NON- CONSER VATIVE	NON- CONSER VATIVE
Arg (785)	(786)
요 1	Arg
ပ	Ø
AGGTCCTCCTCGA A ATTGGGATGGCC[A/GJAGGTGCATCA TCATCATCCCAGA GG	CTCAGACCATGTC C CTTCGGATGCAC[C/G]GTTACAGAGC ACCTGGGGAGCA GGA
	1593
cg44022214 3340	cg43958858
556	557

12 (12p13)	12 (12p13)	12 (12p13)	11 (11922)
0	0	0	2.40E-59
Human Gene SWISSPROT- ID:P22460 VOLTAGE-GATED POTASSIUM CHANNEL PROTEIN KV1.5 (HK2) (HPCN1) - HOMO SAPIENS (HUMAN), 613 aa.	Human Gene SWISSPROT- ID:P22460 VOLTAGE-GATED POTASSIUM CHANNEL PROTEIN KV1.5 (HK2) (HPCN1) - HOMO SAPIENS (HUMAN), 613 aa.	Human Gene SWISSPROT- ID:P22460 VOLTAGE-GATED POTASSIUM CHANNEL PROTEIN KV1.5 (HK2) (HPCN1) - HOMO SAPIENS (HUMAN), 613 aa.	Human Gene Similar to SWISSPROT-ID:P50280 MATRILYSIN PRECURSOR (EC 3.4.24.23) (PUMP-1 PROTEASE) (UTERINE METALLOPROTEINASE) (MATRIX METALLOPROTEINASE- 7) (MMP-7) (MATRIN) - RATTUS NORVEGICUS (RAT), 267 aa.
potassium_ channel	potassium_ channel	potassium_ channel	protease
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Leu (787)	Gly (788)	Ala (789)	His (790)
-B	Arg	Pro	Asp
 -	g	g	O
⋖	O	O	O
CGCTTTGAGACG CAGCTGGGCACC C[AT]GGCGCAGT TCCCCAACACACT	GGGGACGAGGC C CATGGAGCGCTT C[C/G]GCGAGGAT GAGGCTTCATTA AAGA	CATTAAAGAAGAG GAGAAGCCCTG C/GJCCCGCAACG AGTTCCAGCGCC	TGGAGGGGATGC TCATTTTGATGAA[G/C]ATGAAAGGTG GACCAACAATTTC AG
641	898	910	868 868
cg42534568	cg42534568	cg42534568	cg43154190
558	559	560	561

11 (11922)	6 (6pter)	10
2.40E-59	1.60E-124 6 (6pter)	0
Human Gene Similar to SWISSPROT-ID:P50280 MATRILYSIN PRECURSOR (EC 3.4.24.23) (PUMP-1 PROTEASE) (UTERINE METALLOPROTEINASE) (MATRIX METALLOPROTEINASE- 7) (MMP-7) (MATRIN) - RATTUS NORVEGICUS (RAT), 267 aa.	Human Gene Homologous to SWISSPROT-ID:P16083 NAD(P)H DEHYDROGENASE (QUINONE) 2 (EC 1.6.99.2) (QUINONE REDUCTASE) (DT-DIAPHORASE) (AZOREDUCTASE) (PHYLLOQUINONE REDUCTASE) (MENADIONE REDUCTASE) - HOMO SAPIENS (HUMAN), 231 aa.	Human Gene TREMBLNEW-ID:G2725625 ACETOLACTATESYNTHASE - HOMO SAPIENS (HUMAN), 632 aa.
protease	reductase	synthase
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Thr (791)	Cys (792)	Glu (793)
Arg	<u>Ş</u>	Gly
O	—	 -
O	O	O
GATGAAAGGTGG ACCAACAATTTCA[G/C]AGAGTACAACTTTGCTGTTGCGTGTTGCGGTTGCGGTTGCGGTTGCGGTTGCGGTTGCGGTTGCGTGTTGCGGTTGCGTGTTGCGGTTGGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTGCGTGTTG	ATTCTACGATTCC GGTTTGCTCCAG[G/T]GTAAACTAGC GCTCCTTTCCGTA AC	CGCTGCCTTCTCC CGAAAGGTCTGCI C/TJCCTTCACGCG TTCGGCTTCCCGC AG
	694	1081
cg43154190 923	cg43927549	cg43325541
562	263	564

7.40E-65	7.40E-65
Human Gene Similar to SWISSNEW- 7.40E-65 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATE-COA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa. pctryl-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATE-COA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA LIGASE) (ACYL-ACTIVATING ENZYME) - BACILLUS SUBTILIS, 572 aa.	Human Gene Similar to SWISSNEW- 7.40E-65 ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATE-COA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa. pols:SWISSPROT-ID:P39062 ACETYL-COENZYME A SYNTHETASE (EC 6.2.1.1) (ACETATE-COA LIGASE) (ACYL-ACTIVATING ENZYME) (ACETYL-COA SYNTHASE) - BACILLUS SUBTILIS, 572 aa.
synthase	synthase
NON- CONSER VATIVE	NON- CONSER VATIVE
(794)	Thr (795)
Ser	N N
 -	<
U	O
GTGAAGGCATTTG C TGGTCCTGCCTI C/JGCAGTTCCTG TCCCATGACCCAG AA	GACTGTCACAGG GAAAATTCAACGA [G/A]CCAAGCTTC GAGACAAGGAGT GGAA
1474	1617
cg43064068 1474	cg43064068
565	9999

2 (2p21)	2 (2p21)	8 (8p21)	5 (5q35.1)
	0	1.60E-252 8 (8p21)	8.30E-240
Human Gene SWISSPROT- ID:P23945 FOLLICLE STIMULATING HORMONE RECEPTOR PRECURSOR (FSH-R) (FOLLITROPIN RECEPTOR) - HOMO SAPIENS (HUMAN), 695 aa.	FSH-R)) - 695 aa.	Human Gene SWISSPROT- ID:P35348 ALPHA-1A ADRENERGIC RECEPTOR (ALPHA 1A-ADRENOCEPTOR) (ALPHA-1C ADRENERGIC RECEPTOR) - HOMO SAPIENS (HUMAN), 466 aa.	Human Gene SWISSPROT- ID:P21728 D(1A) DOPAMINE RECEPTOR - HOMO SAPIENS (HUMAN), 446 aa.
tm7	tm7	tm7	tm7
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Ala (796)	Thr (797)	Cys (798)	Met (799)
Thr	Asn	Arg	<u>a</u>
ග	U	—	O
4	∢	O	O C
GCAAGAAGTTGAT A TATATGACTCAGIA /GJCTAGGGGTCA GAGATCCTCTCTG GC	AAGGCCAACAAC CTGCTCTACATCA[A/C]CCTGAGGC CTTCCAGAACCTT CCC	GAATGTCTTGAGA (ATCCAGTGTCTC) C/TJGCAGAAAGCA GTCTTCCAAACAT GC	TCTCTGGAGAA GATCCAACCCAT[C/GJACACAAAACG GTCAGCACCCAA
1119	535	1475	1590
cg36988276 1119	cg36988276	cg32296848	cg2524739
567	568	569	570

			1	
				3 (3q25)
8.50E-199	1.40E-196	2.50E-160		2.20E-207
/Е \T) - 364 аа.	Human Gene TREMBLNEW-ID:G2736282 G PROTEIN COUPLED RECEPTOR - HOMO SAPIENS (HUMAN), 362 aa.	Human Gene TREMBLNEW-ID:E1246031 OLFACTORY RECEPTOR - HOMO SAPIENS (HUMAN), 312 aa.	Human Gene Similar to SWISSPROT-ID:P30975 TACHYKININ-LIKE PEPTIDES RECEPTOR 99D (DTKR) - DROSOPHILA MELANOGASTER (FRUIT FLY), 519 aa.	Human Gene SWISSPROT- ID:P26022 PENTAXIN-RELATED PROTEIN PTX3 PRECURSOR (TUMOR NECROSIS FACTOR- INDUCIBLE PROTEIN TSG-14) - HOMO SAPIENS (HUMAN), 381 aa.
tm7	tm7	tm7	tm7	tnf
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
lle (800)	Gly (801)	Ser (802)	Thr (803)	Leu (804)
Thr	Ser	Phe	<u>a</u>	Met
I	O	O	O	F
U	⋖	F	-	∢
AGTGTCTGGATGA C TCTTGTGGTCA[C //IJGCATCCGTTT TCACAAATGGGCT	CATCTTCTCCATC AACCTCTTCAGC[A/G]GCATTTTCTT CCTCACGTGCATG	TCTTTTGTGGACA TCTGCTTCTCT[T /C]CACCACCGTCC CCAAGATGCTGG	GGCCCTGAGAGC AACACCACGGGC A[1/C]CACAGCCTT CTCCATGCCCAG CTGG	TGGAAGCGTGCA TCCAGTGAGACCA [A/TJTGAGGCTTGA GTCTTTTAGTGCC TG
394	519	285	89	8889
cg2320320	cg43264978	cg3003708	cg38841806	cg43336100
571	572	573	574	575

8		19 (19p13.3)	12
.30E-55		4.30E-275	1.70E-177 12
5 TNF CEPTOR ENS	transcriptfac Human Gene SPTREMBL-ID:Q14872 METAL-REGULATORY TRANSCRIPTION FACTOR - HOMO SAPIENS (HUMAN), 753 aa.	transcriptfac Human Gene SWISSPROT- ID:P35269 TRANSCRIPTION INITIATION FACTOR IIF, ALPHA SUBUNIT (TFIIF-ALPHA) (TRANSCRIPTION INITIATION FACTOR RAP74) - HOMO SAPIENS (HUMAN), 517 aa.	transcriptfac Human Gene SPTREMBL-ID:Q07279 TRANSCRIPTION FACTOR NF-E2 - MUS MUSCULUS (MOUSE), 373 aa.
tnfreceptor	transcriptfac tor	transcriptfac tor	transcriptfac tor
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Pro (805)	His (806)	Phe (807)	Leu (808)
Leu	Tyr	nen	Phe
O	O	F	O
F	∢	O	O
GAGGCGCGGGGA GCCAGGCCTGGG C[T/C]CCGGGTCC CCAAGACCCTTGT GCTC	ACTCGCACGTGG ATCCTGAGGCTGT [A/G]AGAGGTAAG GAAGGCTTTGCCA CAG	CATTGACAGCGA GGCCTCCTCAGC C[C/T]TCTTCATGG CGAAGAAGAAGA CGCC	TGACAGAGCTGTA C CCGTGACATTTT[C /G]CAGCACCTTCG GGATGAATCAGG CA
234	2857	1285	1346
cg43335562	cg43140548 2857	cg43011561	cg43998970
576	22.5	578	579

9 (9934) 9 (9934)
6.50E-192 9 (9q34)
transferase Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 24.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) SAPIENS (HUMAN), 354 aa.
transferase
NON- CONSER VATIVE
(803)
ο O
H
O
CACTACTATGTCT C TCACCGACCAGC[C/T]GGCCGCGGT GCCCCGCGTGAC GCTG
464
cg2537639
280

9 (9q34)	
6.50E-192 9 (9q34)	
transferase Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B	
transferase	
NON- CONSER VATIVE	
(810)	
Arg	
O	
O O m	
TCGGCAGCTGTC C AGTGCTGGAGGT G[C/G]GCGCCTAC AAGCGCTGGCAG GACGT	
523	
cg2537639 523	
581	

9 (9934)	
6.50E-192 9 (9q34)	
transferase Human Gene SWISSPROT- ID:P1642 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (NAGAT) - HOMO SAPIENS (HUMAN), 354 aa.	
transferase	
NON- CONSER VATIVE	
(811)	
Phe	
۷	
-	
GGTGTGCGTGGA T CGTGGACATGGA G[7/A]TCCGCGGC CACGTGGGCGTG GAGAT	
cg2537639 643	

9 (9q34)
6.50E-192 9 (9q34)
transferase Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37 (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (NAGAT) - HOMO SAPIENS (HUMAN), 354 aa.
transferase
NON- CONSER VATIVE
(813)
ren
⋖
U
CAAGGACGAGGG C CGATTTCTACTACTAC[C/A]TGGGGGGGT TCTTCGGGGGGGT CGGT
793
cg2537639 793
284

9 (9934)	15	3 (3p25)
6.50E-192 9 (9q34)	0	0
transferase Human Gene SWISSPROT- ID:P16442 FUCOSYLGLYCOPROTEIN ALPHA- N- ACETYLGALACTOSAMINYLTRANS FERASE (EC 2.4.1.40) (HISTO- BLOOD GROUP A TRANSFERASE) (A TRANSFERASE) / FUCOSYLGLYCOPROTEIN 3- ALPHA- GALACTOSYLTRANSFERASE (EC 2.4.1.37) (HISTO-BLOOD GROUP B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B TRANSFERASE) (B SAPIENS (HUMAN), 354 aa.	Human Gene SWISSPROT-ID:004671 P PROTEIN (MELANOCYTE-SPECIFIC TRANSPORTER PROTEIN) - HOMO SAPIENS (HUMAN), 838 aa.	Human Gene SWISSPROT- ID:P31641 SODIUM- AND CHLORIDE-DEPENDENT TAURINE TRANSPORTER - HOMO SAPIENS (HUMAN), 620 aa.
transferase	transport	transport
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
(814)	Asp (815)	Met (816)
Name	Ala	<u>e</u>
⋖	⋖	<u>o</u>
O	O	U
GTTCTTCGGGGG GTCGGTGCAGGA G[G/A]TGCAGCGG CTCACCAGGGCC TGCCA	CACATCGTGGTG GAGCTGACCCAG G[C/A]TGACGCTTT GGGCTCCAGGTG GCGG	GTCTGAAAGATTT CCACAAGGACAT[C/G]CTGAAGCCCT CACCAGGGAAGA GCC
826	3249	427
cg2537639	cg42742340	cg41653463
585	586	587

5 (5p15.3)	5 (5p15.3)	6	17	10 (10q25)
G	0	0	0	0
Human Gene SWISSPROT- ID:Q01959 SODIUM-DEPENDENT DOPAMINE TRANSPORTER (DA TRANSPORTER) (DAT) - HOMO SAPIENS (HUMAN), 620 aa.	Human Gene SWISSPROT- ID:Q01959 SODIUM-DEPENDENT DOPAMINE TRANSPORTER (DA TRANSPORTER) (DAT) - HOMO SAPIENS (HUMAN), 620 aa.	Human Gene SPTREMBL- ACC:Q16084 P130 - HOMO SAPIENS (HUMAN), 1139 aa.	Human Gene SWISSPROT- ACC:P42694 HYPOTHETICAL PROTEIN KIAA0054 - Homo sapiens (Human), 1942 aa.	Human Gene SWISSNEW- ACC:P46013 ANTIGEN KI-67 - Homo sapiens (Human), 3256 aa.
transport	transport	UNCLASSI	UNCLASSI	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
His (817)	Ser (818)	Pro (819)	Arg (820)	Тгр (821)
Asp	Phe	Ala	Gly	ren
ပ	O	9	O	o o
ග	F	U	O	-
CAAGITCACCAAC AACTGCTACAGG[G/CJACGCGATTGT CACCACCTCCATC AA	TCCTCCGGCTTCG TCGTCTTCTCT[T /C]CCTGGGGTACA TGCCACAGAAGC AC	CTGCGGTAGCTG TCCCAGGCCTCG G[C/G]CCGCGCCG CCTCGTCCATGTT GAGG	GCATAGGACATG GCGGGCTTGCCC C[C/G]CGCAGAGC TCTGGGGGCTAC TGTGGGGGCTAC	CAACCCCTAGAAG ACCTGGCTGCT[T/G]GAAAGAGCTC TTCCAGACACCAG TT
1165	1232	4776	522	4604
cg40351913	cg40351913	cg43955093	cg43055918	cg43968854
588	589	590	591	592

4 (4q22)				
0	0	o	0	0
Human Gene SWISSPROT- ACC:P55157 MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN, LARGE SUBUNIT PRECURSOR - Homo sapiens (Human), 894 aa.	Human Gene SPTREMBL- ACC:Q15840 ZINC FINGER PROTEIN BASONUCLIN - HOMO SAPIENS (HUMAN), 994 aa.	Human Gene SPTREMBL- ACC:Q15840 ZINC FINGER PROTEIN BASONUCLIN - HOMO SAPIENS (HUMAN), 994 aa.	Human Gene SPTREMBL- ACC:Q15840 ZINC FINGER PROTEIN BASONUCLIN - HOMO SAPIENS (HUMAN), 994 aa.	Human Gene SPTREMBL- ACC:Q15840 ZINC FINGER PROTEIN BASONUCLIN - HOMO SAPIENS (HUMAN), 994 aa.
UNCLASSI	UNCLASSI FIED	UNCLASSI	UNCLASSI	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Leu (822)	His (823)	Cys (824)	Tyr (825)	lle (826)
Phe	Gln	Ser	Asn	Asn
<u></u>		H	<u> </u>	—
-	O	∢	⋖	٨
CCATTGTTCAAGA CATCCTACGTTIT /GJGAAATGCCTGC AAGCAAAATTGTC C	ACAATTCAGAGAG GGAGACTGAGCA[G/TJACACCAGCAT TGATCATGGTGCC AA	ATCAGGAAAGGT GTTGGATCACTGG [A/T]GCATCATGAC CAGTGAGGAAGA AGT	CCCCAAACAGGA AGTCCATGGGCC C[A/T]ACCCTGACA GCAGCTTCTTAAC	CCCAAACAGGAA GTCCATGGGCCC A[A/T]CCCTGACA GCAGCTTCTTAAC TTCC
1841	2001	553	937	938
cg43070241	cg43262121	cg43262121	cg43262121	cg43262121
593	594	595	596	597

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	6 (6q14)	o		2 (2cen)
0	9.1e-313	2.00E-301	6.10E-236	3.00E-227 2 (2cen)
Human Gene SWISSPROT- ACC:P02771 ALPHA- FETOPROTEIN PRECURSOR (ALPHA-FETOGLOBULIN) (ALPHA- 1- FETOPROTEIN) - Homo sapiens (Human), 609 aa.	Human Gene SWISSPROT- ACC:P21589 5'-NUCLEOTIDASE PRECURSOR (EC 3.1.3.5) (ECTO- NUCLEOTIDASE) (5'-NT) (CD73 ANTIGEN) - Homo sapiens (Human), 574 aa.	Human Gene SWISSNEW- ACC:P42568 AF-9 PROTEIN - Homo sapiens (Human), 568 aa.	Human Gene SWISSNEW- ACC:043913 ORIGIN RECOGNITION COMPLEX SUBUNIT 5 - Homo sapiens (Human), 435 aa.	Human Gene SWISSPROT- ACC:P09529 INHIBIN BETA B CHAIN PRECURSOR (ACTIVIN BETA-B CHAIN) - Homo sapiens (Human), 407 aa.
UNCLASSI	UNCLASSI	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Gly (827)	Thr (828)	Ser (829)	Arg (830)	Ala (831)
Glu	Ala	Ala	Gly	Ser
<u> </u>	4	<u> </u>	A	U
∢	O	o ص	O	4
CTGGAAGAACTTT GCCATGAGAAAGI AGJAATTTTGGAG AAGTACGGACATT CA	AATGATTAACAAC AACCTGAGACAC! G/AJCGGATGAAAT GTTCTGGAACCAC GT	GCCCCCAGGCAT GGCTAGCTCGTG T[G/T]CCGTGCAG GTGAAGCTGGAG CTGGG	CAGCTTTCCATCC ATTTTATTTAT[G/ AJGACATACTGCT AGTGGAAAGACCT A	CAGGTGTCCTGC GAGCCACCCGGG G[A/C]TCCGGGTG GCGGGGGTGGCG
501	1235	367	223	3034
cg44024279	cg44928804	cg43317253	cg41637661	cg42913861
598	599	009	601	602

2		12
1.40E-188 15	4.20E-150	3.70E-142 12
UNCLASSI Human Gene SWISSPROT- ACC:P09471 GUANINE NUCLEOTIDE-BINDING PROTEIN G(O), ALPHA SUBUNIT 1 - Homo sapiens (Human), 353 aa.	UNCLASSI Human Gene Homologous to SWISSPROT-ACC:P14207 FOLATE RECEPTOR BETA PRECURSOR (FR-BETA) (FOLATE RECEPTOR 2) (FOLATE RECEPTOR, FETAL/PLACENTAL) (PLACENTAL FOLATE-BINDING PROTEIN) (FBP) - Homo sapiens (Human), 255 aa.	Human Gene Homologous to SWISSPROT-ACC:P21583 STEM CELL FACTOR PRECURSOR (SCF) (MAST CELL GROWTH FACTOR) (MGF) (C-KIT LIGAND) - Homo sapiens (Human), 273 aa.
UNCLASSI	UNCLASSI FIED	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Gly (832)	Arg (833)	Gly (834)
Ser	Ser	Arg
<u>o</u>	O	O
4	4	4
AGAGGAGAGAGC A CGCCCTCGAGCG G[A/G]GCAAGGCG ATTGAGAAAAACC TCAA	GCCAGAGTTGCA GCATCAGGGCCA G[A/C]CTGAGCAG GAGACCCCCAGT CCCAT	TAGGAATGACAGC A AGTAGCAGTAAT[A/G]GGAAGGCCA AAAATCCCCCTGG AGA
526	335	787
cg43249389 526	cg43919239	cg41642952
603	604	605

	10	9	n
1.60E-134 1	6		2.90E-87
Human Gene Homologous to SWISSNEW-ACC:P08637 LOW AFFINITY IMMUNOGLOBULIN GAMMA FC RECEPTOR III-1 PRECURSOR (FC- GAMMA RIII) (FCRIII) (IGG FC RECEPTOR III-1) (FC-GAMMA RIII-ALPHA) (CD16) (FC-GAMMA RIII-ALPHA) (CD16)	Human Gene Homologous to SWISSPROT-ACC:P50539 MAX INTERACTING PROTEIN 1 (MXI1 PROTEIN) - Homo sapiens (Human), 228 aa.	Human Gene Similar to TREMBLNEW-ACC:AAD38008 GLYOXALASE-I (EC 4.4.1.5) - HOMO SAPIENS (HUMAN), 184 aa.	Human Gene Similar to SWISSPROT-ACC:P49913 ANTIBACTERIAL PROTEIN FALL-39 PRECURSOR (FALL-39 PEPTIDE ANTIBIOTIC) (ANTIMICROBIAL PROTEIN CAP-18) (LL-37) - Homo sapiens (Human), 170 aa.
UNCLASSI FIED	UNCLASSI FIED	UNCLASSI	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Ser (835)	??? (836)	Ala (837)	Asn (838)
Arg	Ser	ng Gl	Thr
O	σ	g	⋖
O	O	-	O
TGTTCCTGGAGCC G TCAATGGTACAG[G/C]GTGCTCGAG AAGGACAGTGTG ACTC	GGGCACAGAAAC ACAGCAGCGGA G[C/S]AGCAACAC CAGCACTGCCAA	ATTGCCATTGTGG TAACTCTGGGTC T/GJCATCATCTTC AGTGCCCCAATTG	GTGAAGCGGTGT ATGGGGACAGTG A[C/A]CCTCAACCA GGCCAGGGGCTC CTTT
221	391	1609	521
cg43945147	cg43926002	cg43972311	cg42556108
909	607	809	609

	T			
	4			14 (14q11.2)
2.30E-85	2.80E-73	5.90E-64	5.90E-64	1.00E-59
Human Gene Similar to SWISSPROT-ACC:P01282 VASOACTIVE INTESTINAL PEPTIDE PRECURSOR (VIP) - Homo sapiens (Human), 170 aa.	Human Gene Similar to SPTREMBL- 2.80E-73 ACC:Q94218 CODED FOR BY C. ELEGANS CDNA CM10H5 - CAENORHABDITIS ELEGANS, 589 aa.	Human Gene Similar to SPTREMBL- 5.90E-64 ACC:O76087 GAGE-8 - HOMO SAPIENS (HUMAN), 117 aa.	Human Gene Similar to SPTREMBL- 5.90E-64 ACC:O76087 GAGE-8 - HOMO SAPIENS (HUMAN), 117 aa.	Human Gene Similar to REMTREMBL-ACC:G238693 T CELL RECEPTOR VARIABLE ALPHA CHAIN - HOMO SAPIENS (HUMAN), 143 aa (fragment).
UNCLASSI FIED	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Pro (839)	Phe (840)	Val (841)	Val (842)	Arg (843)
Gin	\alpha	Met	Met	Gly
ပ	—	O	o	O
⋖	9	V	V	o
AGTGACTTCAGTA AACTCTTGGGTC[A/CJACTTTCTGCC AAAAAGTACCTTG	CGGTATAACGTCA AAAATCCTGTTT[G //IJCAGCCAAGGT TCAGAAATTGCCT C	AAGGCGCTATGTA A CAGCCTCCTGAA[A/GJTGATTGGGCC TATGCGGCCCGA GCA	TGAAGATGGTCCT GATGGGCAGGAG[A/G]TGGACCCGC CAAATCCAGAGGA GGT	ATTACTGAAGGGT GGAGAACAGAAG G/C]GTCATGAAAA AATATCTGCTTCA TT
487	1052	283	505	260
cg36842490	cg43942549	cg42381630	cg42381630	cg3004395
610	611	612	613	614

1.20E-58	1.60E-54	1.60E-54	1.60E-54	1.60E-54
UNCLASSI Human Gene Similar to SWISSNEW- 1.20E-58 ACC:076070 GAMMA-SYNUCLEIN (PERSYN) (BREAST CANCER- SPECIFIC GENE 1 PROTEIN) - Homo sapiens (Human), 127 aa.	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).	Human Gene Similar to REMTREMBL-ACC:G33509 T CELL RECEPTOR - HOMO SAPIENS (HUMAN), 118 aa (fragment).
UNCLASSI FIED	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI FIED	UNCLASSI
NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE	NON- CONSER VATIVE
Glu (844)	Gln (845)	Met (846)	Gin (847)	Ser (848)
\sqr	ren	 	Leu	Phe
-	⋖	⋖	A	U
A	H-	O	⊢	F
CACTTCCTCTTTC TCTTTGGATGCC[A/T]CACCCTCCTG TTGGGGGGCAGA	GAAGACAAGGTG GAAGACAAGCCCTC [T/A]ATCTCTGGTT GTCCACGAGGGA GAC	TGTAACTCTCAAT TGCAGTTATGAA G/AJTGACTAACTT TCGAAGCCTACTA	GAAGTGACTAACT TTCGAAGCCTAC(T/AJATGGTACAAG CAGGAAAAGAAA GCT	AGCATATTAGATA AGAAAGAACTTITI /CJCAGCATCCTGA ACATCACAGCCAC C
733	289	342	364	475
cg43960645 733	cg2526759	cg2526759	cg2526759	cg2526759
615	616	617	618	619

(17q21.3 2)	17 (17q21.3 2)	
D	i i	1.80E-157
Human Gene SWISSPROI - ID:P08514 PLATELET MEMBRANE GLYCOPROTEIN IIB PRECURSOR (GPIIB) (INTEGRIN ALPHA- IIB) (CD41) - HOMO SAPIENS (HUMAN), 1039 aa.	Human Gene SWISSPROT- ID:P08514 PLATELET MEMBRANE GLYCOPROTEIN IIB PRECURSOR (GPIIB) (INTEGRIN ALPHA- IIB) (CD41) - HOMO SAPIENS (HUMAN), 1039 aa.	Human Gene SWISSNEW- ID:Q08722 LEUKOCYTE SURFACE ANTIGEN CD47 PRECURSOR (ANTIGENIC SURFACE DETERMINANT PROTEIN OA3) (INTEGRIN ASSOCIATED PROTEIN) (IAP) (MER6) - HOMO SAPIENS (HUMAN), 323 aa.pcls:SWISSPROT-ID:Q08722 LEUKOCYTE SURFACE ANTIGEN CD47 PRECURSOR (ANTIGENIC SURFACE DETERMINANT PROTEIN OA3) (INTEGRIN ASSOCIATED PROTEIN) (IAP) (MER6) - HOMO SAPIENS (HUMAN), 323 aa.
cadherin	cadherin	cadherin
FRAMES HIFT	FRAMES HIFT	HIFT HIFT
His (849)	His (850)	(851)
T d	Pro	Arg
<u>o</u>	⋖	d e b
gap	gap	H
TACAGAATATGTC gap GTCGGTGCCCCC[gap/C]ACTTGGAG CTGGACCCTGGG AGCGG	GTCGGCTTCTTCA AGCGGAACCGGC[gap/A]CACCCCTG GAAGAAGATGATG AAGA	GTCCATCACTTCA CTTCAGTTATTC[T/ gap]CCTAGGAGGT TGTATAGTCTTCT GA
1067	3285	2521
cg40310734	cg40310734	cg43956660
620	621	622

2			(11923)	15 (15q15)
			1.80E-203	0
Human Gene SWISSPROT- ID:P12111 COLLAGEN ALPHA 3(VI) CHAIN PRECURSOR - HOMO SAPIENS (HUMAN), 3176 aa.	Human Gene SPTREMBL- ID:Q92804 PUTATIVE RNA BINDING PROTEIN RBP56 - HOMO SAPIENS (HUMAN), 592 aa.	Human Gene SPTREMBL- ID:Q92804 PUTATIVE RNA BINDING PROTEIN RBP56 - HOMO SAPIENS (HUMAN), 592 aa.	Human Gene SWISSNEW- ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa. pcls:SWISSPROT-ID:P06727 APOLIPOPROTEIN A-IV PRECURSOR (APO-AIV) - HOMO SAPIENS (HUMAN), 396 aa.	glycoprotein Human Gene SWISSPROT- ID:P16452 ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.
collagen	dna_rna_bi nd	dna_rna_bi nd	u de	glycoprotein
FRAMES collagen	FRAMES	FRAMES HIFT	FRAMES	FRAMES
Gly (852)	Arg (853)	Leu (854)	Asp (855)	Asn (856)
Gly	Arg	Tyr	r L	Thr
<u> </u>	9	O	O	⋖
gap	gap	gap	gap	gap
CTCCAGGGATAGT gap TGGACAGAGGG[gap/GJAGACCCTG GCTACCCAGGAC	GCTATGGAGGCA (AAATGGGAGGAA GIgap/GJAAACGAC TACAGAAATGATC AGCGC	CGGTTACTCCAGT TATGGACAAAGT[g ap/CJTATTCACAGT CCTATGGTGGTTA TG	GGCCGAGCAGCT GCGCGCCCAGCT G[gap/G]ACCCCCT ACGCACAGCGCA TGGAGA	CAGACTTCCACAG AGTGCTGGATGA[gap/A]CGCGGCCT GCCTTGCCCCAG GGTTA
2429	1837	263	584	1553
cg43970982	cg42175288	cg42175288	cg41554010	cg43065549
623	624	625	626	627

			- 1
14 (14q11.2)			0.
9.90E-70 14 (14)	1.20E-224 7	1.40E-261 6	9.60E-262 20
FRAMES glycoprotein Human Gene Similar to SWISSPROT-ID:P16452 HIFT ERYTHROCYTE MEMBRANE PROTEIN BAND 4.2 (P4.2) (PALLIDIN) - HOMO SAPIENS (HUMAN), 690 aa.	Human Gene SWISSPROT- ID:P50219 HOMEOBOX PROTEIN HB9 - HOMO SAPIENS (HUMAN), 401 aa.	Human Gene SWISSPROT- ID:P15260 INTERFERON-GAMMA RECEPTOR ALPHA CHAIN PRECURSOR (CDW119) - HOMO SAPIENS (HUMAN), 489 aa.	Human Gene SPTREMBL- ID:Q15802 SERINE/THREONINE PROTEIN KINASE KRS-2 - HOMO SAPIENS (HUMAN), 487 aa.
glycoprotein	homeobox	interferon	Kinase
FRAMES HIFT	FRAMES	FRAMES interferon HIFT	FRAMES HIFT
Leu (857)	Arg (858)	End (859)	His (860)
ne	Pro	ren	<u></u>
U	O	gap	O
gap	gap	⋖	gap
TGACCACGGGGT GCTGGATGCCTG C[gap/C]TTATACAT CCTGGACCGGCG GGGGA	GCGCCGCGAGAC AAGGGCAGCGGA C[gap/G]CGCCTGC GGACTTGAGGGA CAGTGA	ATAAGTTACAATG CTTTTTTGTTT[A/ gap]AAAAAAAAAAAAAAAAAAAAAAAAAGTCTGTACTTTTTTTT	CTGTGGGGCTGG TTCTGTATCTGATI gap/CJATCATTCGA TTACGAAATAAAA CGT
666	1220	364	379
cg41568631	cg41637704	cg43933380	cg43072541
628	629	630	631

2 (2q13)	19	19	1 (1033)
2.40E-82	9.70E-214	9.70E-214	0
Human Gene Similar to SWISSPROT-ID:P25155 COAGULATION FACTOR X PRECURSOR (EC 3.4.21.6) (STUART FACTOR) (VIRUS ACTIVATING PROTEASE) (VAP) - GALLUS GALLUS (CHICKEN), 475 aa.	Human Gene SWISSPROT- ID:P01137 TRANSFORMING GROWTH FACTOR BETA 1 PRECURSOR (TGF-BETA 1) - HOMO SAPIENS (HUMAN), 390 aa.	Human Gene SWISSPROT- ID:P01137 TRANSFORMING GROWTH FACTOR BETA 1 PRECURSOR (TGF-BETA 1) - HOMO SAPIENS (HUMAN), 390 aa.	Human Gene SWISSPROT- ID:Q03167 TGF-BETA RECEPTOR TYPE III PRECURSOR (TGFR-3) (BETAGLYCAN) - HOMO SAPIENS (HUMAN), 849 aa.
protease	Jō ₁	tgf	tgfreceptor
FRAMES HIFT	FRAMES	FRAMES	FRAMES
Leu (861)	Ala (862)	Ala (863)	Ala (864)
ਜੂ ਹ		nen	Ala
<u> </u>	o	O	O
gap	gap	gap	gap
GTCAGCCGCTAC CTCGACTGGATCC [gap/T]ATGGGCAC ATCAGAGACAAG GAAGC	CCGGGCAGAGCT GCGTCTGCTGAG G[gap/G]CTCAAGT TAAAAGTGGAGCA GCACG	CCGGGCAGAGCT GCGTCTGCTGAG G[gap/G]CTCAAGT TAAAAGTGGAGCA GCACG	AATCTCCGCACTG gap CAGGCCAGGGGC Igap/CJTGGCCAGC TACAGAGAGAGG
1536	1317	1317	847
cg44032168	cg43931248	cg43931248	cg43272560
632	633	634	635

5.20E-254 3	1.40E-182
Human Gene SWISSPROT- ID:P32241 VASOACTIVE INTESTINAL POLYPEPTIDE RECEPTOR 1 PRECURSOR (VIP-R- 1) (PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE TYPE II RECEPTOR) (PACAP TYPE II RECEPTOR) (PACAP-R-2) - HOMO SAPIENS (HUMAN), 457 aa.	Human Gene SWISSPROT- ID:P53611 GERANYLGERANYL TRANSFERASE TYPE II BETA SUBUNIT (EC 2.5.1) (RAB GERANYLGERANYLTRANSFERAS E BETA SUBUNIT) (RAB GERANYL GERANYLTRANSFERASE BETA GERANYLTRANSFERASE BETA SUBUNIT) (RAB GG TRANSFERASE) (RAB GGTASE) - HOMO SAPIENS (HUMAN), 331 aa.
tm7	FRAMES transferase
FRAMES tm7	FRAMES
(865) (865)	Pro (866)
Gly	Oln
H	O
deb	gap
CCAGGATCCATTT gap TGAGGATTATGG[gap/T]GTGCTGGG ACACCATCAACTC CTCA	CAAATCCCCCGT gap TTCTTCATCTTG[g ap/GJACATGCTAA AATGAAATTACGC AGT
	625
cg43266471 1067	cg43995237
936	637

~	×	7	7
1.40E-182	6.40E-257	3.80E-252	3.80E-252
	<u>ဖ</u>		
Human Gene SWISSPROT- ID:P53611 GERANYLGERANYL TRANSFERASE TYPE II BETA SUBUNIT (EC 2.5.1) (RAB GERANYLGERANYLTRANSFERAS E BETA SUBUNIT) (RAB GERANYL GERANYLTRANSFERASE BETA SUBUNIT) (RAB GG TRANSFERASE) (RAB GGTASE) - HOMO SAPIENS (HUMAN), 331 aa.	Human Gene SWISSPROT-ACC:P78539 SUSHI REPEAT-CONTAINING PROTEIN SRPX PRECURSOR - Homo sapiens (Human), 464 aa.	Human Gene SWISSNEW- ACC:Q13228 SELENIUM-BINDING PROTEIN 1 - Homo sapiens (Human), 472 aa.	Human Gene SWISSNEW- ACC:Q13228 SELENIUM-BINDING PROTEIN 1 - Homo sapiens (Human), 472 aa.
FRAMES transferase	UNCLASSI	UNCLASSI FIED	UNCLASSI
FRAMES HIFT	FRAMES	FRAMES	FRAMES
Phe (867)	Arg (868)	Leu (869)	Gly (870)
ren	Arg	Pro	Gly
O	ග	gap	gap
gap	gap	ග	ڻ ق
TTCTTCATCTTGA CATGCTAAAATG[g ap/G]AAATTACGC AGTTTCTCTCTAT CAA	CCGCCTCTGCTG (CTGCTGCTGCTGCTGCTGCTGCTGCTCCCCGCGCGCGCG	ATCCAGGCTGAG CTGGATCATCTGA [G/gap]GGCCTCCA GCCACCCGTTTTC	CCAGGCTGAGCT GGATCATCTGAG G[G/gap]CCTCCAG CCACCCGTTTTCC CTTGA
938	267	965	299
cg43995237 (cg43254094	cg44034555	cg44034555
638	639	640	641

	(1p36.2)	(9q22.2)	20	0.7
1.00E-251	1.00E-201	3.50E-178	3.20E-147	3.20E-147
NDING 3P) - aa.	Human Gene SWISSPROT- ACC:P18615 RD PROTEIN - Homo sapiens (Human), 380 aa.	Human Gene SWISSPRO1- ACC:P09467 FRUCTOSE-1,6- BISPHOSPHATASE (EC 3.1.3.11) (D-FRUCTOSE-1,6- BISPHOSPHATE 1- PHOSPHOHYDROLASE) (FBPASE) - Homo sapiens (Human), 337 aa.	Human Gene Homologous to SPTREMBL-ACC:Q15182 SNRNP POLYPEPTIDE B - HOMO SAPIENS (HUMAN), 285 aa.	Human Gene Homologous to SPTREMBL-ACC:Q15182 SNRNP POLYPEPTIDE B - HOMO SAPIENS (HUMAN), 285 aa.
UNCLASSI		UNCLASSI	UNCLASSI FIED	UNCLASSI
FRAMES	FRAMES HIFT	FRAMES	FRAMES HIFT	FRAMES HIFT
Gly (871)	Asp (872)	Gly (873)	Leu (874)	Phe (875)
\alpha	Asp	dig O	Pro	Phe
ග	U	dag	gap	gap
gap	gap	O	9	O
AGCGAGTCCTCC GGGAGGCCCACA G[gap/G]TTACTGC CTCCAGCTGCAG	CGTTCCAGAGGA GCATATCTGCTGA [gap/CJTGATGACC TGCAAGAGTCATC CAGA	GGAACTCGAGCA CGTCGTCGGGGG A[C/gap]CCCAAGA TCACCGGCGCCC TCTGGT	ATTCCCGGGGGA (GGGGGCCCTGTA A[G/gap]GGAAACC AGACAATCCCATG	TCCCGGGGGAGG GGGCCCTGTAAG G[G/gap]AAACCAG ACAATCCCATGAG
882	379	306	195	197
cg39711096	cg44128902	cg43946951	cg43948890	cg43948890
642	643	644	645	646

	5 (5q23			5		5
3.20E-143	1.00E-107 5 (5q23)		2.50E-72	5.80E-50		5.80E-50
Human Gene Homologous to TREMBLNEW-ACC:AAD43025 PTD017 - HOMO SAPIENS (HUMAN), 258 aa.	Human Gene Homologous to SWISSNEW-ACC:Q99075 HEPARIN-BINDING EGF-LIKE GROWTH FACTOR PRECURSOR (HB-EGF) (HBEGF) (DIPHTERIA TOXIN RECEPTOR) (DT-R) - Homo		Human Gene Similar to SPTREMBL-ACC:060869 EDF-1 PROTEIN -HOMO SAPIENS (HUMAN), 148 aa.	Human Gene Similar to TREMBLNEW-ACC:AAD38944 NJAC PROTEIN - HOMO SAPIENS	(HUMAN), 99 aa.	Human Gene Similar to TREMBLNEW-ACC:AAD38944 NJAC PROTEIN - HOMO SAPIENS (HUMAN), 99 aa.
UNCLASSI FIED	UNCLASSI FIED	JOON JONE	FIED	UNCLASSI FIED		UNCLASSI
FRAMES	FRAMES	FRAMES	HIFT	FRAMES HIFT		FRAMES HIFT
Pro (876)	Glu (877)	<u>^</u>	(878)	Asp (879)	300	(880)
Ala	Asp	<u>≥</u>		Gly	2	<u> </u>
gap	O	gap)	gap	ממ) 1
O	gap	ပ		9	_©)
GGGCCTGTCTGC CCAGTGGAGGAG G[C/gap]TTCCGCT GGTGTTCTAGGG	CTCTCGGCACTG GTGACTGGCGAG Algap/GJCCTGGAG CGGCTTCGGAGA GGGCTA	TCGTGGCCAGGT	CCTTCTGCGTAAG [C/gap]CCCTTGCT CTGCCGACCTTG CTGGA	GGTCCAAATGCAA GTGCTCCCGGAA[G/gap]GGACCCAA GATCCGCTACAG	CGACG TCCAAATGCAAGT	GCTCCCGGAAGGI G/gapJACCCAAGA TCCGCTACAGCG ACGTG
713	373	681		450	452	
cg43917524 713	cg43942004	cg43932428		cg44010855	cg44010855	
647	648	649		650	651	

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CGGGAGCTCT GCCAGCTTTG GCGAACGAGG GTGCTTGCCT CGTGCCCCTT G
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 Asn Thr Arg Leu Leu Cys His Val Met Leu Cys Leu Leu Gly
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 Gly Ser Thr Val Ile Ala Gly Ser Ile Asn Ala His Gly Ser
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Tyr Ala Glu Arg Tyr Gln Met Pro Thr Gly Ile Lys Gly Pro
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Asn Pro Leu Val Pro Gly Thr Pro Gly Arg Pro Gly Ile Pro
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Gly Ser Leu His Pro His Pro Pro Tyr His Ile Arg Val Ala
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Leu Tyr Ser Arg Leu Gly Gly Gln Pro Val Tyr Leu Pro Thr
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Gln Ser Val Val Ser Cys Ala End Ala Pro Gln Ser Gly Leu
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Ala Phe Val Val Leu Ala Leu Gln Phe Leu Ser His Asp Pro
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Asn Asn Leu Leu Tyr Ile Thr Pro Glu Ala Phe Gln Asn Leu
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Leu Arg Ile Gln Cys Leu Cys Arg Lys Gln Ser Ser Lys His
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Leu Glu Lys Ile Gln Pro Met Thr Gln Asn Gly Gln His Pro
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Trp Met Ile Phe Val Val Ile Ala Ser Val Phe Thr Asn Gly
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 Val His Pro Val Arg Pro Leu Arg Leu Glu Ser Phe Ser Ala
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Tyr Val Phe Thr Asp Gln Leu Ala Ala Val Pro Arg Val Thr
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Leu Ser Val Leu Glu Val Gly Ala Tyr Lys Arg Trp Gln Asp
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 Phe Gly Thr Leu His Pro Ser Phe Tyr Gly Ser Ser Arg Glu
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Lys Asp Phe His Lys Asp Met Leu Lys Pro Ser Pro Gly Lys
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Gly Phe Val Val Phe Ser Ser Leu Gly Tyr Met Ala Gln Lys
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Ser Glu Arg Glu Thr Glu His Thr Pro Ala Leu Ile Met Val
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 Lys Val Leu Asp His Trp Cys Ile Met Thr Ser Glu Glu Glu
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Lys Gly Glu Gln Lys Arg His Glu Lys Ile Ser Ala Ser
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Glu Tyr Val Val Gly Ala Pro His Leu Glu Leu Asp Pro Gly
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Phe Phe Lys Arg Asn Arg His Thr Pro Gly Arg Arg End End
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Thr Ile Gln Pro Pro Arg Glu End Leu
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Gly Ile Val Gly Gln Lys Gly Arg Pro Trp Leu Pro Arg Thr
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Gly Gly Lys Met Gly Gly Arg Lys Arg Leu Gln Lys End Ser
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Tyr Ser Ser Tyr Gly Gln Ser Leu Phe Thr Val Leu Trp Trp
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Glu Gln Leu Arg Arg Gln Leu Asp Pro Leu Arg Thr Ala His
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Ser Thr Glu Cys Trp Met Asn Ala Ala Cys Leu Ala Pro Gly
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Thr Asp Phe Phe Phe End Thr Lys Lys Ala Leu End Leu
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       <211> 14
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       <400> 860
       Gly Ala Gly Ser Val Ser Asp His His Ser Ile Thr Lys End
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       <210> 861
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Arg Tyr Leu Asp Trp Ile Leu Trp Ala His Gln Arg

His Gly Val Leu Asp Ala Cys Leu Ile His Pro Gly Pro Ala

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Ala Glu Leu Arg Leu Leu Arg Ala Gln Val Lys Ser Gly Ala
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Pro His Cys Arg Pro Gly Ala Trp Pro Ala Thr Glu Arg Gly
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Ile His Phe Glu Asp Tyr Gly Val Leu Gly His His Gln Leu
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Leu Leu Leu Leu Leu Arg Arg Pro Ala Gln Pro Gln Leu
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 Lys Arg Val Ala Gly Gly Leu Arg End Ser Ser Ser Ala Trp
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Ser Ser Gly Arg Pro Thr Gly Tyr Cys Leu Gln Leu Gln Gln
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 Gln Arg Ser Ile Ser Ala Asp End End Pro Ala Arg Val Ile
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 Arg Ala Pro Val Ile Leu Gly Pro Pro Thr Thr Cys Ser Ser
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Leu Met Gly Leu Ser Gly Phe Leu Thr Gly Pro Pro Pro
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Pro Arg Thr Pro Ala Glu Pro Pro Pro Leu Gly Arg Gln Ala
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Gly Thr Gly Asp Trp Arg Glu Pro Gly Ala Ala Ser Glu Arg
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       <211> 14
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       <220>
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and the semi semi semi semi
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       Lys Cys Lys Cys Ser Arg Lys Asp Pro Arg Ser Ala Thr Ala
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       Cys Lys Cys Ser Arg Lys Asp Pro Arg Ser Ala Thr Ala Thr
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